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A TWENTY-FIVE YEAR EVALUATION OF THE TREATMENT OF CARCINOMA OF THE CERVIX WITH IRRADIATION*

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THE Uterine Cancer Follow-up Clinic was established in the Department of Gynecology of the Jefferson Medical College Hospital on Sept. 1, 1921, as a division of the Outpatient Department. The purpose was to follow systematically the progress of all patients seen and/or treated for uterine malignancy. With the merger of the Department of Gynecology and the Department of Obstetrics in 1946, the work has been continued in the Division of Gynecology and is now designated as the Pelvic Malignancy Follow-up Clinic because patients with all types of pelvic cancer are included in the census, which is also an integral part of the Tumor Clinic of the hospital. The senior author has been privileged to work in the clinic since its inception by the late Dr. Brooke M. Anspach, then Professor and Head of the Department of Gynecology at Jefferson.

Material

The present report continues in the tradition of four previous ones regarding patients seen and treated for carcinoma of the cervix, and published successively in 1931,[1] 1936,[2] 1942,[3] 1949.[4] Separate reports relating to

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cancer of the corpus have also been published.[5-10] This, the fifth report on cervical carcinoma from our clinic, is unique in that we can now evaluate a twenty-five year series—548 patients seen and/or treated from Sept. 1, 1921, to Sept. 1, 1946, and, therefore, eligible for five-year evaluation. A high percentage of follow-up has always characterized the reports from the Jefferson Clinic; relatively few patients have been lost sight of. In the present report the follow-up figure is 98.5 per cent. Only eight of the 548 patients seen are untraced, and four of these eight patients were followed from eight to eighteen years before they were lost.

There is much of historical interest in this study, covering as it does our awakened consciousness that emphasizes early diagnosis, the significance of noninvasiveness, and the evolution of therapy. The previous reports emphasized cumulative experience and included in the end results all types of therapy. Since our management has been predominantly by irradiation, this twenty-five year summation will concern itself primarily with that type of therapy as we have used it. In this respect, we acknowledge the benefit of a rich experience to draw upon, because the progressive changes instituted in the technique used throughout a twenty-five year period lend themselves to rational evaluation. We believe this to be true since our policy has been to work with a technique at least five years before altering it appreciably. In that way one can analyze and judge accomplishments to far better advantage and with more certainty.

Previously, we have included in our relative results those patients treated primarily elsewhere (Group V, Schmitz). While this is statistically acceptable for absolute figures, it is not exactly fair or sufficiently informative in so far as relative results or evaluation of changing techniques is concerned. Hence, this report will exclude such patients in computing the relative survival figures.

During the past few years we have gradually and as accurately as possible re-evaluated our Schmitz grouping on the basis of the League of Nations classification as modified in the more recent International Classification at present so widely accepted. For our records, however, we are retaining both classifications for each patient. This has proved interesting from a comparative viewpoint, especially since all the previous reports were based entirely upon the Schmitz nomenclature.

Reclassification from the Schmitz grouping has not been an easy task when reviewing case histories of a thirty-year period. But this is not surprising when we consider that in the *Annual Report on the Results of Radiotherapy in Carcinoma of the Uterine Cervix, Volume VI,* 1951, various contributing institutions report a variation in their total number of cases of from 3.6 to 36.9 per cent in Stage I and from 16.5 to 49.9 per cent in Stage II. Heyman explains this disparity on the basis of selectivity. With Stage I and IV patients our task has been reasonably simple; the difficulty arises in re-evaluating Groups II and III. From the original descriptions, the great majority of Group II patients (Schmitz) were placed in Stage I (International). All in all, the figures for Group I (Schmitz) and Stage I (International) favor a greater percentage in the latter, while Stage II (International) figures have greatly reduced the percentage of Group III (Schmitz) patients. Any appreciable error might well be explained by the character of broad ligament involvement in Group III (Schmitz) patients that could easily have been mistaken for extending malignant disease, since in either case there might be no demonstrable space between the cervical lesion and the lateral bony pelvic walls. Furthermore, the presence or absence of involved regional nodes in these stages and groups cannot, of course, be determined by palpation. In fact, who can determine

without visualization what the nodal situation is in any stage of the disease? Recoveries and survival rates in Stage III cases would lend weight to the conclusion that nodes were uninvolved or perhaps influenced by irradiation. On this basis, we have 73 patients (15.1 per cent) in Stage I, 275 patients (56.8 per cent) in Stage II, 89 patients (18.3 per cent) in Stage III and 48 patients (9.9 per cent) in Stage IV (Table I).

TABLE I. CARCINOMA OF CERVIX. OVER-ALL FIVE-YEAR RESULTS IN PATIENTS PRIMARILY TREATED AT JEFFERSON MEDICAL COLLEGE HOSPITAL IRRESPECTIVE OF METHOD, 1921-1946

INTERNATIONAL				PERCENTAGE SURVIVAL				SCHMITZ			
STAGE	SEEN	TREATED	SURVIVAL	ABSOLUTE	RELATIVE	RELATIVE	ABSOLUTE	SURVIVAL	TREATED	SEEN	GROUP
I	73	72	40	54.7	55.5	56.0	56.0	8	14	14	I
II	275	273	90	32.7	32.9	50.0	50.0	32	64	65	II
III	89	83	4	4.5	4.8	27.1	27.4	92	334	340	III
IV	48	35	0	0.0	0.0	3.1	3.9	2	51	66	IV
Total	485	463	134	27.6	28.8	28.8	27.6	134	463	485	

FOLLOW-UP, 98.5 PER CENT

Figures relating to age incidence, parity, and race have shown little if any variation as the series of patients has increased throughout the observation period of twenty-five years (Tables II and III). Still, of clinical importance is the figure of 27 per cent of cervical cancer cases occurring in women 40 years of age and younger. The greatest incidence of cervical carcinoma, however, is in the fifth decade. Our youngest patient was 22 months of age[11]; the youngest adult was 22 years of age and the oldest adult was 79 years of age. Table II also reflects age incidence in relation to survival rate. It is noteworthy that the survival rate including all methods of therapy is fairly uniform for each decade and approximates closely the over-all survival rate recorded in Table I.

TABLE II. AGE INCIDENCE AND RELATION TO FIVE-YEAR SURVIVAL RATE, 1921-1946

AGE (YEARS)	SEEN	PERCENTAGE	SURVIVAL	PERCENTAGE
1- 9	1	0.2	0	0.0
10-19	0	0.0	0	0.0
20-29	18	3.7	4	22.2
30-39	99	20.4	26	26.3
40-49	156	32.1	51	32.6
50-59	128	26.4	34	26.5
60-69	72	14.8	18	25.0
70- +	11	2.3	1	0.9
Total	485		134	27.6

That women of the Hebrew race are less susceptible is borne out by the recent comprehensive article of Kennaway of London.[12] In our clinic 1.2 per cent of the total are in Jewish women, and this is in accord with the findings of the above-mentioned author. Table III depicts racial incidence in relation to survival rate. Here again, with the exception of the Hebrew race, the survival rate is fairly uniform, but with only six Hebrew women in our series, a statistically significant survival rate cannot be obtained for them alone. Also, 9.9 per cent of the patients were nulliparous and this also seems to have little influence on survival rates (Table III).

The histologic incidence remains practically unchanged from previous reports. Twenty-eight of the 485 cases of cervical malignancy seen primarily

at Jefferson were adenocarcinomas, an incidence of 5.7 per cent. The remainder were of the squamous-cell variety. During the same period of 1921 to 1946, there were 77 cases of endometrial carcinoma on the ward service. Thus, in our series at least, malignancy of the cervix occurs 6.3 times as frequently as endometrial malignancy. The peak incidence of endometrial carcinoma occurs later in life than that of cervical carcinoma, most endometrial carcinoma in our experience being found in women over 50 years of age.

TABLE III. RACIAL INCIDENCE AND PARITY RELATION TO FIVE-YEAR SURVIVAL RATE, 1921-1946

	SEEN	PERCENTAGE	SURVIVAL	PERCENTAGE
Race.—				
White	414	85.3	117	28.2
(Gentile)	408	84.1	114	27.9
(Hebrew)	6	1.2	3	50.0
Negro	71	14.7	17	23.6
Parity.—				
Nullipara	48	9.9	12	25.0
Parous	431	88.6	121	28.1
Unknown	6		1	
Total	485		134	27.6

Diagnosis and the Delay Period

A generation ago Howard Kelly propounded how simple the treatment of cervical cancer would be if the diagnosis were made early. He appealed for the prompt examination of women who had "spotting" or irregular vaginal bleeding of any sort, urging biopsy of abnormall areas and prophylactic care of the abnormal cervix. Only within the past decade, however, has the public been made more forcibly conscious of their own responsibility in the early diagnosis of cancer. The propaganda of the American Cancer Society, the Public Health Service, enthusiastic lay groups, and organized medicine at all levels has created a demand that the individual physician, including the general practitioner, be alert to his responsibility in this matter of early diagnosis.

How has this insistence on early diagnosis been reflected in our own experience? We believe that in the past five years we have seen an appreciable increase in Stage I lesions. In Philadelphia, the Committee for the Study of Pelvic Cancer has been valiant in its efforts to awaken the physician as well as the patient to the danger of ignoring symptoms that may mean pelvic cancer. The reports of J. Y. Howson,[13, 14] the Chairman, and his colleagues are worthy of reading by all physicians. Briefly, monthly discussions are held at the Philadelphia County Medical Society, where physicians—general practitioners and specialists alike—are invited to discuss those cases of pelvic cancer in which the presence or absence of delay periods has been established by the Committee's investigators who interrogate hospitalized pelvic cancer patients. Table IV illustrates the appalling delay period still existent today, and points out the need for more work of this sort. From September, 1945, to June, 1951, 2,418 patients with pelvic cancer, admitted to hospitals for treatment, were studied. Note that in only 28.8 per cent (697 cases) was there no delay period in diagnosis and subsequent treatment. In 15.5 per cent (374 cases) the delay was the physicians'. In 38.8 per cent (937 cases) the delay was due to the patient. Both patient and physician were responsible in 15.0 per cent (347) cases and institutional delay was apparent in 0.9 per cent (22 cases). Surely, statistics such as these offer more than food for thought in the importance of

early diagnosis, viz., early attention to symptoms, prompt examination with suitable diagnostic procedures, and institution of appropriate therapy. However, the importance of periodic health-maintenance examinations must not be minimized.

TABLE IV. PHILADELPHIA COMMITTEE FOR THE STUDY OF PELVIC CANCER, DELAY PERIOD, 1945-1951

Patients studied	2,418
DELAY	PERCENTAGE
Patient	38.8
Physician	15.5
Physician and patient	15.0
Institutional	0.9
None	28.8

The early and continued efforts of Macfarlane and her group testify to the good results of such a program.[15] Another is the instruction of the physician, from medical school to postgraduate levels, in proper methods of diagnosis. Here the Schiller test, the Papanicolaou smear, and perhaps the sponge biopsy have a place in the investigation of the abnormal, and, to some extent, of the normal-appearing cervix. *But none of these measures replaces a meticulous history and pelvic examination with adequate biopsy if the cervix is suspicious.* Microscopic tissue confirmation of cancer is still the final court for cancer diagnosis. Finally, and what seems to us rational and sensible, is the prophylactic treatment of the abnormal cervix, for to put the diseased cervix in good condition is surely logical. In our clinic we prefer and recommend the "circular biopsy" followed by endothermic resection.[16] By this method a long-handled scalpel is utilized to excise a collar of tissue from around the external os. By the use of the knife, rather than the cutting current, uncharred tissue is removed. As many radial sections as practical are studied and the parts unused kept on appropriate file in the laboratory. Any particularly suspicious area may be marked with a pin. With this method the complete squamocolumnar junction, the site of the origin of most cervical carcinoma, is removed and available for thorough analysis. The healed cervix that results reduces a potential health hazard. This is a hospital procedure but in no way conflicts with taking "spot" biopsies of suspicious-looking areas on the cervix as a clinic or office procedure. However, there is greater probability of discovering an early lesion, or even a controversial noninvasive one, by the "circular biopsy" method. If malignancy is not found, the end result is pleasing in that a normal-appearing cervix results. Postoperative stenosis is prevented by periodic dilatations. A thorough curettage of the entire endometrial cavity and cervical canal should accompany the cervical biopsy. We also practice the so-called fractional curettage, curetting first the cervical canal, then the uterine cavity. This is done mainly to locate the exact location when canal or corpus carcinoma are to be differentiated.

A few remarks about diagnostic aids as the result of our experience can be rather succinctly stated. Careful history taking and meticulous examination are of basic importance; this cannot be emphasized too often. Nor can the dictum of routine periodic pelvic examinations be overstressed. In our clinic we teach that any asymptomatic woman in the second and third decades should be checked gynecologically at least once yearly. Beyond that age, six month examinations are in order. Friability must never be ignored, either on the portio or where it is so often not looked for, in the cervical canal.

Broad ligament or uterosacral thickening, or localized fixation may be significant even though the uterus as a whole seems fairly mobile. A careful digital rectal examination, in conjunction with the bimanual pelvic one, is an important aid in examination, since broad ligament induration is more easily detected this way. Combined rectovaginal examination is of value especially in detecting uterosacral and posterior vaginal wall infiltration. One should also examine breasts and all regional nodal areas that are accessible. We have not used the colposcope as advocated by Hinselmann.[17] Schiller's test using dilute aqueous iodine (Lugol's solution) applied to the cervix is only valuable in pointing out areas of abnormal epithelization, but its suggested use as a diagnostic aid certainly makes more physicians cancer conscious. The sponge biopsy[18] has not been employed in our clinic.

Our use of the cytologic method of Papanicolaou has been extensive and in the past six years smears have been taken on selected outpatients and nearly all inpatients. Smears are now taken on all carcinoma cases before, during, after treatment, and at each follow-up visit. The more smears one obtains the better, and, whenever possible, we take vaginal and cervical scrapings and endocervical smears. Our best results with the smear technique have been in those patients whose symptomatology suggests cancer. In the asymptomatic patient with negative pelvic findings only occasionally have we discovered a suspicious smear later confirmed as cancer by biopsy. On the other hand, repeated doubtful or suspicious smears call for immediate curettage and biopsy. Of great interest has been ultimate discovery of ovarian or tubal malignancy in four patients whose smears were abnormal, suggesting malignancy. Treatment for carcinoma is instituted only on the basis of biopsy; a positive smear in our opinion is insufficient evidence.

Our experience with the Papanicolaou smear is summarized in Table V. Smears were taken before therapy was begun in 94 patients. In 85 cases, or 90.4 per cent, the smears were reported as positive, suspicious, or doubtful. In each of these patients, the examining physician suspected cancer of the cervix because of the history or clinical appearance of the cervix. In 9 instances, or 9.6 per cent (false positives), the smear was reported as showing no evidence of malignancy. False positives average less than one per cent, but false negatives may reach 10 per cent.

TABLE V. INITIAL PAPANICOLAOU SMEARS IN PROVED CASES OF CARCINOMA OF CERVIX

PATIENTS		PERCENTAGE
Positive	5	5.3
Suspicious	75	79.8
Doubtful	5	5.3
Negative	9	9.6
Total	94	90.4

Evolution in Therapy

In general, irradiation therapy at Jefferson has undergone three distinct phases in principle:

1. 1921 to 1936: Radium locally (massive dose technique), sometimes with subsequent x-ray, occasionally with x-ray prior to radium applications. This comprises a fifteen to twenty-five year evaluation period.

2. 1935 to 1942: Preliminary x-ray followed in three to four weeks by radium applications with technical changes in x-ray factors and radium screening: a seven to fifteen-year evaluation period.

3. 1942 to 1951: Vaginal cone therapy added to preliminary x-ray technique, followed by radium locally; a five-year evaluation period of patients treated prior to Sept. 1, 1946, patients subsequently treated not being eligible for five-year evaluation.

It is obvious that the evaluation of some patients extends beyond the exact time limits stated with respect to the three progressive alterations in technique. However, a sufficient number of patients have been treated and observed in each of the above categories to present reliable survival statistics for comparative evaluation and comment.

Total hysterectomy of the conventional pattern was completely abandoned as a primary method of treatment in 1923. The relatively few patients in whom surgery played a part in treatment offer no material for comparative study, for in each instance radium and x-ray were also used. During the past three to five years surgery has played an inconspicuous role in that only two Wertheim procedures, each preceded by x-ray irradiation, have been carried out, chiefly because of complicating pelvic pathology (i.e., fibromyomas in Stage I lesions). Postirradiation extraperitoneal iliac lymphadenectomy is being done whenever good local results have occurred after complete irradiation therapy with x-ray and radium. None of these patients, however, are yet eligible for five-year evaluation. Their status will be mentioned later in the paper. No surgery has been performed on so-called radioresistant patients as evidenced by local appearance, biopsy, and Papanicolaou smear studies. Of great interest are two patients in this series who were operated upon because of abdominal masses ten years after irradiation therapy. In each instance a granulosa-cell tumor of an ovary was removed but no residual evidence of cervical carcinoma was found. These cases were reported in a discussion of a paper by Novak and Jones[19] at a meeting of the American Gynecological Society in 1939.

Five cases of carcinoma in situ occur in our series. These cases have been followed carefully from one to seven years. They have not been subjected to surgery other than circular biopsy or given any irradiation therapy. Repeat cervical biopsies have been performed in each case, and in each instance the recent biopsy has shown no involvement. This group is being carefully and frequently followed. Their subsequent course should prove enlightening. A retrospective study of this controversial subject is now in progress, and, by this study, a case of carcinoma in situ, reported by the author as such in a discussion of Te Linde and Galvin's[20] paper at the American Gynecological Society meeting in 1948, has been re-evaluated with more cuts from the original block and is now believed to be truly invasive.

Results of Treatment and Irradiation

In Table I we have presented the over-all five-year results obtained with irradiation therapy irrespective of the techniques employed in patients seen and treated primarily by us. The results are expressed in both absolute and relative percentages,* showing an over-all survival rate of 28.8 per cent. Both the International and Schmitz classifications are shown for comparison.

In Table VI we show the results (absolute and relative) observed in 63 patients who were primarily treated elsewhere, whether with surgery, irradiation, or a combination of both by the previous therapists.

*Absolute survival rate means the percentage of patients living five years or more after therapy based on the total number of patients seen (treated and untreated). Relative survival rate refers to the percentage of patients living five years or more after therapy based on the total number of patients treated.

TABLE VI. CARCINOMA OF CERVIX. PRIMARY TREATMENT ELSEWHERE IRRESPECTIVE OF METHOD, SO-CALLED GROUP 5 SCHMITZ, 1921-1946

SEEN	STATUS	SURVIVAL	PERCENTAGE
63	18 Observed only	4	22.2
	45 Re-treated (irradiation)	6	13.3

Sixty-five patients were treated with x-ray only (Table VII). All but two patients had far-advanced cases, were treated palliatively, and subsequent radium application was not advisable. The two Stage I patients, paradoxically enough, have survived ten and fourteen years, respectively. The former exhibited tuberculosis and cancer in the biopsy, had a positive serology, and failed to return for further treatment after completion of external irradiation. Traced assiduously, she was found and examined two years ago, seen recently, and found free of disease. The second patient refused complete x-ray and radium treatment, but shows no evidence of unarrested cancer.

TABLE VII. CARCINOMA OF CERVIX. FIVE-YEAR RESULTS, X-RAY PRINCIPALLY, VAGINAL CONE OCCASIONALLY, 1921-1946

INTERNATIONAL			PERCENTAGE SURVIVAL		SCHMITZ		
STAGE	TREATED	SURVIVAL	REL.	REL.	SURVIVAL	TREATED	GROUP
I	2	2	100.0	100.0	1	1	I
II	17	0	0.0	100.0	1	1	II
III	22	0	0.0	0.0	0	34	III
IV	24	0	0.0	0.0	0	29	IV
Total	65	2	3.1	3.1	2	65	

Table VIII is concerned with, and depicts the results obtained with, irradiation in the early days of the clinic. Between 1921 and 1936, radium was regarded as the keystone of treatment; in fact, until 1931 it was used almost exclusively, with x-ray therapy reserved for far-advanced cases only. Eight per cent of these patients were re-irradiated with radium two or three times. About 1931 and for a few years thereafter, external irradiation began to be used as a supplementary procedure following radium. This group shows a 27.9 per cent five-year survival rate. Later, in 1936, we began using x-ray prior to radium, and this program became more widely followed from then on, as will be noted in succeeding Table IX. Note that the survival rate rose then to 34.6 per cent.

TABLE VIII. CARCINOMA OF CERVIX. FIVE-YEAR RESULTS, RADIUM PRINCIPALLY, X-RAY SPORADICALLY, 1921-1936

INTERNATIONAL			PERCENTAGE SURVIVAL		SCHMITZ		
STAGE	TREATED	SURVIVAL	REL.	REL.	SURVIVAL	TREATED	GROUP
I	28	15	53.5	75.0	3	4	I
II	147	45	34.6	41.4	12	29	II
III	42	2	4.6	26.2	47	179	III
IV	5	0	0.0	0.0	0	10	IV
Total	222	62	27.9	27.9	62	222	

During the period covering 1921 to 1936 the radium available was a 50 mg. capsule of radium sulfate enclosed in a glass capsule and screened with 0.3 mm. of silver and 1.0 mm. of brass and 2 cm. active length. This was enclosed in black rubber tubing of 2.0 mm. thickness for intracervical application. Also

available at the same time were needles of 2 cm. length containing 12.5 mg. of radium sulfate screened with 0.3 mm. of monel metal for interstitial application about the periphery of the lesion. Thus, we had available for massive dose treatment 150 mg. of radium. The distribution of the capsule and needles was decided upon empirically by the operator, and the dosage expressed in milligram hours. Beginning with 2,000 to 2,200 mg. hr., the time of implantation was increased to as high as 4,300 mg. hr. in 1927-1928, but reduced to an average dosage of 3,600 mg. hr. in the latter year. In 1935 another 50 mg. of radium sulfate screened with 0.5 mm. of platinum was obtained for use additionally with intrauterine application when a tandem application in conjunction with the brass capsule was desired. It was not until 1938 that the available armamentarium of radium was changed entirely, as will be noted later.

With respect to external irradiation: from 1921 to 1927 massive dosage was given in single applications at right angles to three or four pelvic ports. The amount given was what the skin would tolerate and the treatment was completed in three or four days. The factors were 3 Ma., 170 to 200 kv., filtration 0.5 mm. copper and 1.00 mm. aluminum, 50 cm. skin target distance; ports 16, 19, and 20 cm. square. The delivered dosage per port varied from 800 to 2,100 r. After 1927 the fractional method was adopted, using two anterior and two posterior ports. The object was to deliver 100 per cent of the skin erythema dose to the depths of the pelvis in two weeks on alternate days until the saturation level was reached; then treatment was continued for two more weeks; 1,400 to 1,500 r were delivered through each port.

Table IX includes the period beginning in 1936, and extending to 1942-1943, when preliminary x-ray therapy prior to radium applications became more or less a standardized type of treatment. Naturally, as previously stated, the division in time is not entirely a clear-cut one, but sufficient observation of patients treated in this way permits an evaluation and comparison with the previous and with the succeeding therapy groups (Table IX and Table X). During this epoch, changes occurred in the radium and x-ray factors. Still employing massive dose radium therapy, the radium available was revamped in distribution so that three 50 mg. capsules of 2 cm. length and screened with 1.5 mm. of platinum were made available for tandem application to the cervicouterine canal and to the endometrial cavity. Pararubber tubing was now used to enclose the metal capsules. The old Monel metal needles were replaced with ten 10 mg. needles of 2 cm. length, each screened with 0.5 mm. of platinum for interstitial application. Most of the patients evaluated in Table IX were, therefore, treated with this newer set-up, also in use at present.

TABLE IX. CARCINOMA OF CERVIX. FIVE-YEAR RESULTS, PRELIMINARY X-RAY, SUBSEQUENT RADIUM, NO VAGINAL CONE, 1936-1942-43

INTERNATIONAL			PERCENTAGE SURVIVAL		SCHMITZ		
STAGE	TREATED	SURVIVAL	REL.	REL.	SURVIVAL	TREATED	GROUP
I	18	10	55.6	50.0	2	4	I
II	75	26	34.6	53.3	8	15	II
III	12	1	8.3	30.6	26	85	III
IV	2	0	0.0	33.3	1	3	IV
Total	107	37	34.6	34.6	37	107	

The x-ray methods previously noted were likewise changed somewhat. Although the filtration factors remained the same, the manner of treatment was altered, in 1938-1939 so that the portal therapy was extended from three to

four weeks for completion with two anterior and two posterior ports; two such areas were treated daily, each receiving 200 r (measured in air), and continued until a well-marked erythema was obtained, occurring in general with a total of 1,600 to 2,400 r to each area. Three to four weeks later the massive dosage with radium was given, the therapy averaging 3,600 to 4,800 mg. hr., and this part of the technique remains in vogue as just stated.

The physical factors of the x-ray machines have not changed essentially since about 1937, namely, 200 kv., 25 Ma., skin target distance usually 50 cm., sometimes 80 cm. with thick individuals, and half-value layer of approximately 0.9 mm. of copper.

Since 1946 the external air dosage per port has tended to increase. We are now attempting to achieve a parametrial dose of 3,500 r in a period of about five weeks. This dosage is calculated as the summation of the midplane contributions from one anterior and one opposing posterior port.

No attempt has been made to calculate the total radium dosage at any precise points in the pelvis. Such figures represent rather gross approximations under the best conditions and are actually misleading when applied in retrospect to cases in which roentgen proof of the true positions of the tubes and needles is lacking. Films are now being taken routinely after all radium applications and work being undertaken in our new Radiation Physics Laboratory should make these data available in the study of future cases.

The external irradiation has always been carried out with the close cooperation of the Department of Radiology. From 1921-1943 the external irradiation was given under the supervision of the late Drs. Willis Manges, Manges Smith, and Karl Kornbloom. Since 1943 Dr. Paul Swenson and Dr. Theodore Eberhard have been supervising this phase of the therapy.

TABLE X. CARCINOMA OF CERVIX. FIVE-YEAR RESULTS, PRELIMINARY X-RAY, VAGINAL CONE, RADIUM (PLANNED THERAPY), 1942-3-1946

INTERNATIONAL			PERCENTAGE SURVIVAL		SCHMITZ		
STAGE	TREATED	SURVIVAL	REL.	REL.	SURVIVAL	TREATED	GROUP
I	20	11	55.0	33.3	1	3	I
II	34	19	55.8	58.8	10	17	II
III	7	1	1.4	52.7	19	36	III
IV	4	0	0.0	11.1	1	9	IV
Total	65	31	47.6	47.6	31	65	

Table X depicts what has been accomplished since the technique was altered for the third time, in 1942, when a vaginal port of application was added. With this technique, the survival rate has been 47.6 per cent. It has been used whenever technically possible, even in some Stage IV cases, and has been continued as a planned type of therapy. Several sizes of cones are used, dependent upon the vaginal capacity. It has been noted that in some instances the subsequent contracture makes radium application more difficult than before the use of this port. It has been observed that the surface of the lesion is considerably altered in appearance, so much so that one would almost be inclined to forego treatment with radium. However, dilatation of the cervix and the insertion of needles usually reveals a continued, though often unsuspected, friability, with active cancer cells observed both in Papanicolaou smears and by biopsy. Hence, we feel that external irradiation, with cone therapy added, cannot be relied upon alone, for local cancerocidal action; radium must be used to complete the treatment for direct attack on the local lesion.

The present three- and four-year trend with this present type of therapy is encouraging:

Of 13 patients observed for four years, 9 are alive (69.2 per cent) without local evidence of disease.

Of 29 patients observed for three years, 16 are alive (55.2 per cent) without local evidence of disease. This discrepancy in the three-year survival trend is being carefully studied because of recently increased x-ray dosage and other factors. Also, during this three- and four-year period two patients were submitted to the Wertheim type of hysterectomy after preliminary irradiation, because both of them had large fibromas complicating a Stage I lesion of the cervix. Nodes were not found involved. In addition, ten patients have also had bilateral extraperitoneal lymphadenectomy performed after completion of the planned therapy resulted well locally. Only one of them showed carcinomatous involvement of the removed nodes.

Table XI presents in summary the progressive improvement that has occurred with the establishment of a planned type of therapy, and particularly since vaginal cone therapy was added in 1942. Whether or not irradiation will ultimately take care of concomitant nodal involvement is a controversial question. We do know that nodal involvement in the clinically "early" case can take place alarmingly early. It is speculative as to whether radical surgery in such instances offers a better chance of survival; apparently it does not in most instances reported. Lymphadenectomy after apparently satisfactory irradiation therapy must be viewed in the same light for this procedure, too, has definite limitations, since, early or late, metastasis to nodes distant from the pelvis is not rare. Hence, if irradiation is to be relied upon, it has to be brought to a higher state of efficiency by improved localization of points of intensity and more accurate inclusion of tributary nodal zones.

TABLE XI. CARCINOMA OF CERVIX. FIVE-YEAR RESULTS, COMPARATIVE EVALUATION 1921-1946

METHOD	TREATED	SURVIVAL	PERCENTAGE
Radium principally X-ray sporadically 1921-1936	222	62	27.9
Preliminary x-ray Subsequent radium No vaginal cone 1936-1942-3	107	37	34.6
Preliminary x-ray Vaginal cone Subsequent radium 1942-3-1946	65	31	47.6
X-ray principally Vaginal cone occasionally 1921-1946	65	2	3.1
Surgery and/or x-ray and radium 1921-1923	4	2	50.0
Total	463	134	28.8

Carcinoma of the Cervical Stump

A few words are in order about our results in the treatment of cervical stump carcinoma, which are summarized in Table XII.

Of the patients recorded, most of them probably had cancer present at the time of the supravaginal hysterectomy. It seems superfluous, in view of

the constant warnings in the literature, to call attention again to the actual and potential danger of permitting the cervix to remain, unless cancer has been carefully excluded beforehand. Furthermore, if it is elected to retain the cervix, it should always be primarily treated by circular biopsy with scalpel followed by endothermic desiccation, not only to obliterate any grade of endocervicitis but in order to have a pathologic report of the cervix as a matter of record. Needless to say, there is also the obligation to perform a curettage of the endometrium and cervical canal as a preliminary procedure, for it is just as easy to overlook carcinoma of the endometrium as cancer of the cervix. While total hysterectomy for benign disease of the uterus is not always indicated, the total operation is in general a far better procedure to carry out whenever possible, especially so in older women, particularly after the age of 40 years.

TABLE XII. CARCINOMA OF CERVICAL STUMP, 1921-1946

Carcinoma cervix treated	463	
Carcinoma cervical stump	21	
Incidence		4.5%
Five-year survival	10	48.0%
Alive or noncarcinoma death	4	19.0%
Died or recurrence (6, 8, 10, 10, 12, 12 years)	6	

Carcinoma of the cervical stump was encountered in 21 of the 463 patients primarily treated in this series—an incidence of 4.5 per cent. Eight of these were from our own service. This is approximately the same incidence reported previously from this clinic.[21] The time interval since the supravaginal hysterectomy varied from six months to twenty-five years. Forty-eight per cent of these patients lived five years after treatment was instituted, but six of these survivors died of carcinoma six to twelve years after treatment.

Complications

In our opinion, the increased five-year survival rates among those patients treated between 1936-1943 (34.6 per cent) and between 1942-1946 (47.6 per cent) result from several factors: (1) a "planned" type of patient preparation and therapy; i.e., preliminary external irradiation followed at a suitable interval by local radium applications; (2) increased dosage of external irradiation, including the use of the additional vaginal port; (3) thoughtful distribution of the intracavitary and interstitial radium application with respect to a calculated "milligram-hour" dosage. (More recently roentgenograms are being made of the radium applications to try and insure improved accuracy of dosage by the estimation of more precise points in the pelvis.)

As might be expected, the increased amount of external irradiation, as previously noted, may well have resulted in a greater percentage of local complications—proctitis, sigmoiditis, cystitis, rectal and bladder fistulas. About 20 per cent of patients have shown some gradations of such complaints, varying from diarrhea and urinary frequency to bowel hemorrhage, obstruction, hematuria, and fistula formation. Nine colostomies have been performed for bowel obstruction or rectal hemorrhage among the patients evaluated in this report, primarily because of irradiation fibrosis.

Table XIII refers specifically to rectovaginal and vesiculovaginal fistulas, and the increased incidence (from 1.9 to 7.6 per cent) bears out the assumption that our most recent planned technique, and the one in vogue at present, reflects a definite rise in irradiation complications, and particularly with respect to fistulas. Hence, a price is being paid for the increased survival rate

shown, justified though it may be. It is incumbent upon us, therefore, to determine more exactly those factors responsible for this postirradiation damage, and that is being done in conjunction with the Department of Radiology and a newly-established Radiation Physics Laboratory so that the more exact dosage methods may be accomplished. In the meantime, it may be advisable to return to a lower external irradiation dosage, and certainly not to persist in the presence of progressive discomfort on the part of the patient during her course of treatment.

TABLE XIII. CARCINOMA OF CERVIX. IRRADIATION COMPLICATIONS, FISTULA, 1921-1946

METHOD OF TREATMENT	NO. PATIENTS	DEVELOPED RECTO-VAGINAL FISTULA	PERCENTAGE	DEVELOPED VESICO-VAGINAL FISTULA	PERCENTAGE
Radium principally X-ray sporadically 1921-1936	222	15	6.8	15	6.8
Surgery and/or X-ray and radium 1921-1923	4	0	0.0	0	0.0
X-ray only 1921-1946	65	0	0.0	2	3.0
Preliminary x-ray Subsequent radium No vaginal cone 1936-1943	107	2	1.9	2	1.9
Preliminary x-ray Vaginal cone Subsequent radium 1942-1946	65	2	3.0	3	4.6
Total	463	19	4.1	22	4.7

FOUR HAD BOTH RECTOVAGINAL AND VESICOVAGINAL FISTULAS.

Comment

This presentation is concerned with a precise and detailed report of our experience with irradiation treatment for carcinoma of the cervix based entirely on a twenty-five year evaluation of patients seen and treated by us primarily. Hence, we feel that it is beyond the scope and intent of our report to include for comparison with our work voluminous quotations and references to the many splendid publications in the literature sponsored by colleagues at home and abroad. Many of these workers are known to us personally; their able efforts, trustworthy reports, and sincere opinions are respected by us, and the knowledge of their experience has been helpful to us. To mention some and not others would be not only ungracious but repetitious.

Neither is this the place to argue for or against the relative merits of the so-called "swing of the pendulum back to surgery." Irradiation and surgery cannot and never should be competitors for the favor of the unfortunate cancer patient. Both agents are allies in the fight to destroy or arrest malignancy, and individualization of the patients should be the pathway of our therapeutic approach. To our minds, one of the most constructive seminars with respect to this controversial problem in treatment took place at the 1951 meeting of the American Gynecologic Society when Meigs[22] presented his outstanding experimental work on radical hysterectomy with bilateral lymph node dissections. The paper, together with the expressed thoughts of the discussants, really epitomizes our present-day thinking, and everyone interested in cervical carcinoma should be familiar with this reference.

Summary

1. An evaluation and critical analysis of the 485 patients seen and/or treated by irradiation for carcinoma of the cervix on the ward service of the Division of Gynecology, Department of Obstetrics and Gynecology at Jefferson Medical College Hospital, from Sept. 1, 1921, to Sept. 1, 1946, have been presented, with a follow-up record of 98.5 per cent.

2. Modification in the evaluation of five-year survival results, as contrasted with previous reports from this service, have been explained.

3. Transposition of all patients from the original Schmitz grouping to the International staging has been accomplished, with both classifications appearing for comparison in the statistical evaluations.

4. The question of the "delay period" in the diagnosis of pelvic cancer in the City of Philadelphia has been presented, with pertinent comment and data.

5. Methods applicable for earlier diagnosis and prophylaxis with respect to cervical carcinoma have been discussed.

6. The progressive evolution in our methods of utilizing irradiation therapy with x-ray and radium since 1921 has been compared with methods described in previous reports and minutely analyzed, revealing increasing five-year survival rates as follows:

A. 1921-1936	27.9 per cent.
B. 1936-1942	34.6 per cent.
C. 1942-1946	47.6 per cent.

7. The three- and four-year trends with the continued use of the "planned therapy" initiated in 1942 have likewise been scrutinized, as well as certain operative procedures that have been performed additionally during the same period.

8. The occurrence of carcinoma of the cervical stump among the patients in this series has been commented upon.

9. Postirradiation complications have been discussed in some detail, indicating that increased survival rates have been accompanied by a higher incidence of bowel and bladder disturbances. Further improvement in irradiation methods is vital if serious damage to normal tissue is to be avoided in an appreciable percentage of patients so treated.

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255 SOUTH 17TH STREET

AN EVALUATION OF INTRAVENOUS PITUITRIN*†

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SINCE the first introduction by intramuscular injection of Pituitrin into obstetrical usage, there has been dissatisfaction with this method of administration. After Kamm and his associates separated Pituitrin into two active components, Pitocin and Pitressin, there was renewed interest in the use of the oxytocic fraction as a means of stimulating uterine contractions in labor. Page,[1] in 1943, employed Pitocin in oil as a means of providing slow absorption and a prolonged action in cases of inertia uteri. The results were not encouraging and he was the first to advocate the intravenous drip method. In England, Theobald[2] reported excellent results with the latter method of administration. Later, other observers, including Hellman,[3] Stone,[4] Lubin and associates,[5] and Cosgrove,[6] reported favorably on the results in clinics in the United States of the administration of Pituitrin by intravenous infusion. Today, throughout the country, Pituitrin is still being administered for the most part by the subcutaneous route, but the intravenous route is becoming more popular. We began the use of Pituitrin by intravenous drip in the latter part of 1948.

Material

In our study of over one thousand cases, Pituitrin is used intravenously in a dilution of 1:1,000 to 1:10,000. In many other clinics, the dilution is more frequently 1:1,000, or a 1 c.c. ampule of Pituitrin to each 1,000 c.c. of diluent. We usually employ 1½ to 2 minims of Pitocin or Pituitrin in 500 c.c. of 5 per cent glucose well dissolved in distilled water or normal saline, in a dispensing bottle delivering 30 drops per minute, or 120 c.c. (½ minim) per hour. If, as rarely occurs, the uterine response is not good, the rate of administration is increased gradually to 60 drops per minute, or 1 minim per hour in 250 c.c. of diluent. In nontoxic patients, normal saline may be employed instead of distilled water. Demerol, or other adequate sedation, must be employed as necessary. Demerol, 100 mg., and scopolamine, $\frac{1}{150}$ grain, may be administered either by slow introduction into the tubing close to the needle through which the Pituitrin infusion is being given, or subcutaneously. In some cases where food has been taken by the patient prior to her admission to the hospital, the rapid intravenous administration of Demerol in 100 mg. dosage causes vomit-

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†This report includes service cases from Cumberland Hospital and St. Catherine's Hospital, and private cases of the authors.

ing, so emptying the stomach and permitting anesthesia to be safely employed later. Demerol in doses of 25 to 50 mg. may be added as necessary and scopolamine may be repeated in a dosage of $\frac{1}{250}$ to $\frac{1}{30}$ grain.

The timely use of Demerol and scopolamine enhances the action of Pituitrin given by intravenous infusion and it does not interfere with labor. The status of the membranes is extremely important, we believe, in determining the success or failure of Pituitrin in the induction of labor. If they are unruptured, results are not good, but with membranes either spontaneously or artificially ruptured, labor will be induced by the establishment of favorable characteristics of uterine contractions (Reynolds, Lubin, Waltman, Delson, and Tisdall, 1950[7]). In clinical practice, it is often observed that uterine contractions appear to accomplish little in the way of progressive dilatation of the cervix when the membranes are intact, but after the membranes rupture spontaneously, rapid dilatation of the cervix takes place. This fact is utilized when we artificially rupture the membranes in indicated cases.

We oppose the administration of Pituitrin subcutaneously because its action is often unpredictable and its effect cannot be controlled once the injection is made. Like any other drug given repeatedly by subcutaneous injection, there are peaks and depressions in effect, depending upon the rate of absorption from the residual deposit within the tissues. With the intravenous route, it is surprising what a small quantity of the oxytocic substance is necessary to complete a labor. Upon withdrawal of the infusion, there is immediate cessation of stimulated uterine activity.

There are many reports in the literature which testify to a number of uterine ruptures following subcutaneous injection of Pituitrin. This is, indeed, a real danger. To the best of our knowledge, to date there have been no reports of rupture of the uterus attributable to the use of intravenous Pituitrin. No doubt with a large increase in the number of patients receiving this oxytocic agent, there will be instances of uterine rupture. However, we feel that, with judicious usage, in controlled hospitals, under the guidance of obstetrical specialists, in properly selected cases, this catastrophe will not occur.

In many hospitals, Pituitrin is administered subcutaneously by the nursing staff in graduated increasing dosage. *With the intravenous route, it is obligatory for the obstetrician to be present at the patient's bedside at all* times to observe the effect on uterine contractions and changes, if any, in fetal heart rate. If the dosage is $\frac{1}{2}$ minim per hour, there is very little chance that abnormal uterine contractions of sufficient intensity to rupture a uterus will result. Changes in the fetal heart rate may be observed very quickly if higher concentrations of Pituitrin are employed. With our very dilute solutions, the fetal heart rate is usually maintained satisfactorily. If the uterine contractions are such that the uterine wall in the fundus is indentable at the acme of pain, no progressive dilatation of the cervix may be anticipated. Early correction of this deficiency is indicated, and, if it is, most gratifying results may be expected.

It is essential that the cervix must be prepared, or "ripe," for labor when intravenous use of Pituitrin is begun. The fully effaced cervix, even if only 2 cm. dilated, is favorable to successful management by intravenous infusion of Pituitrin. The cervix, which is thick, uneffaced, and undilated, is unripe for stimulation by Pituitrin and should not be disturbed. Oftentimes, failures in the use of Pituitrin by intravenous drip are ascribed to just such cases, in which one or more unsuccessful attempts have been made to stimulate labor. The continued administration of Pituitrin in these cases produces uterine contractions and pains but they do not lead to termination of labor. It is our observation that this group of patients offers a contraindication to the use of

Pituitrin. These cases fall into a special group seen most frequently in private practice. They tend to be high strung, nervous, and apprehensive primiparous young individuals who are experiencing a preliminary (prodromal) stage of labor, or they are overimpressed with the intensity of the Braxton Hicks contractions. They may be advised by their families to enter the hospital too early. After one remains in the hospital with painful intermittent uterine contractions for a day or more, the obstetrician, under pressure of the family, may try to stimulate labor. These patients may be kept at home under mild sedation until the contractions are established at a regular frequency of one every three minutees. If these patients appear at the hospital, they should be sent home or given sedation for the night and then sent home. They must not be given Pituitrin until they are in true labor. To persist in the administration of Pituitrin prior to the time when the cervix is favorable to it will result in an increase in the incidence of cesarean section in this so-called uterine inertia. These cases are not to be classified as primary uterine inertia since there has been no true labor. We advocate early use of Pituitrin in prolonged labors. The definition of prolonged labor is not universally agreed upon. Schmitz and co-workers[8] consider that labor lasting more than 24 hours is prolonged, as do Hellman and his associates[9]; Douglas and Stander,[10] 30 hours; Cosgrove and Glisson,[11] 36 hours. In a more recent study, Daro and Gollin[12] consider a primiparous patient to have a prolonged labor after 18 hours, and a multiparous patient, after 12 hours.

We believe that the onset of labor is difficult to determine accurately if judged subjectively on pain alone. Therefore, uterine contractions must be such that they are not only rhythmic and regular but must give rise to progressive dilatation and effacement of the cervix. Excellent results with the judicious application of Pituitrin in over 95 per cent of cases of prolonged labor were reported by Daro and Gollin. Not only were the labors shortened, but the incidence of midforceps and operative deliveries was markedly reduced; the fetal mortality decreased sixfold, and the maternal morbidity decreased fourfold. No estimate of the psychic effect on the patient is mentioned. These prolonged labors occur for the most part in primiparous women and must leave their mark on the patients. The condition undoubtedly contributes to voluntary sterility and one-child marriages.

In order to decrease the incidence of prolonged labor, we believe an appraisal of the type of labor which the patient is experiencing is important. Since the primiparous woman normally should deliver within 18 hours after the onset of labor, the estimated time of delivery is possible from careful observation. If the labor does not appear to be progressive as evidenced by increase in the intensity and duration of the uterine contractions along with the continuous steady dilatation of the cervix, we believe Pituitrin may be judiciously employed. In fact, it is indicated. It is our impression, in these cases which are not progressing satisfactorily, that the intravenous use of Pituitrin results in contractions which are more frequent, greater in intensity, and exhibit fundal contractile dominance. These characteristics result in shorter labors. These features of uterine contractility have been studied by us, using the multichannel tokodynamometer, when Pituitrin is used intravenously during normal labor. If there is delay attributable to decreased efficiency of uterine contractions, early detection and immediate administration of Pituitrin by intravenous drip results in increased incidence of spontaneous rotation of the fetus from the posterior and transverse positions. In a recent publication, a waiting period of two hours in the second stage was advocated. We believe that, if 30 minutes pass without progress in rotation or descent in the second stage of labor, prompt administration of intravenous Pituitrin by

TABLE I. MIDFORCEPS, CUMBERLAND HOSPITAL

	1949		1950		1951	
	CASES	PER-CENTAGE	CASES	PER-CENTAGE	CASES	PER-CENTAGE
Midforceps	32	2.0	20	1.2	8	0.55
Manual rotation	17	1.0	23	1.4	13	0.89
Forceps rotation	27	1.7	14	0.8	17	1.16
Total	76	4.8	57	3.5	38	2.6
Total deliveries	1,566		1,627		1,459	
Percentage decrease in midforceps				27		46

drip is indicated. This method has reduced, to a minimum, the number of manual or instrumental rotations and midforceps deliveries (Table I). If uterine contractions are normal and the progress of labor is slow but steady, no stimulation should be attempted. Some observers believe that an increase in the use of pituitrin by intravenous infusion will result in an increase in fetal and neonatal deaths. That this is not true is shown by the steadily decreasing fetal death rate in our clinics (Table II). Moreover, in all of our experiences, we believe that in only a single case, one of severe toxemia of pregnancy, was there any possible connection between the oxytocic agent and fetal mortality.

TABLE II. INFANT MORTALITY, CUMBERLAND HOSPITAL

Fetal Mortality

	FULL TERM			OVER 1,500 GRAMS			UNDER 1,500 GRAMS			
YEAR	FULL TERM	STILL-BIRTHS	NEO-NATAL	LIVE BIRTHS	STILL-BIRTHS	NEO-NATAL	LIVE BIRTHS	STILL-BIRTHS	NEO-NATAL	TOTAL
1946	835	13	0	90	10	3	14	22	5	41
1947	1,266	19	2	117	6	3	19	14	2	35
1948	1,351	13	4	128	1	1	12	12	5	29
1949	1,397	3	1	126	10	2	8	12	2	22
1950	1,473	19	3	117	4	2	8	14	1	23
1951	1,313	7	2	115	11	2	4	8	10	22

Stillbirth and Neonatal Mortality

INFANTS OVER 1,500 GRAMS

	1946	1947	1949	1950	1951
Total number of live births	928	1,388	1,526	1,595	1,432
Total number of stillbirths	23	25	23	23	18
Rate per 1,000 live births	24.7	18.0	15.0	14.4	12.5
Total number of neonatal deaths	3	5	3	5	4
Rate per 100 live births	3.2	3.6	1.9	3.1	2.8
Total number of stillbirths and neonatal deaths	26	30	26	28	22
Rate per 1,000 live births	27.9	21.6	16.9	17.5	15.3

Indications for Intravenous Pituitrin

The indications and contraindications for the use of Pituitrin by intravenous drip administration, as based on our experience in over 1,000 cases since the latter part of 1948, may be listed as follows:

Indications: (1) Stimulation of labor, (2) induction of labor, (3) cephalopelvic disproportion, relative, (4) breech presentation, average size fetus, (5) parity, not over four, (6) age, no limitation, (7) twins with ruptured mem-

branes, (8) large fetus with adequate pelvis, (9) fetal condition, (10) fetal death, (11) premature separation of placenta, (12) marginal placenta previa.

Contraindications to the use of Pituitrin administered intravenously, based on our experience, are as follows: (1) Contracted pelvis, (2) large breech, (3) high parity with large fetus, (4) twins with overdistention of uterus and intact membranes, (5) previous section or hysterotomy, (6) abnormal presentation, (7) maternal exhaustion, temporary contraindication, (8) general physical condition of patient.

If doubtful about the indication, *do not use.*

1. Stimulation of Labor.—For the most part, ineffectual uterine contractions which annoy the patient without accomplishing any purpose should be eliminated. We believe that uterine contractions, in order to be effective, must be progressively more frequent, longer in duration, stronger in intensity (see Lubin, Reynolds, Waltman, Tisdall, and Delson,[5] 1950), and must effect continuous, steady, and progressive effacement and dilatation of the cervix. Any delay in this process must be detected early in labor. If no progress is made in one to two hours, intravenous fluids (electrolytes plus oxytocic agent) are suggested. We believe it is important to administer the Pituitrin at the earliest detected deficiency in the progress of labor rather than to wait four, six, or eight hours, as some observers suggest.

2. Induction of Labor.—For success to be achieved in this group of cases, proper selection is mandatory. The cervix must be ripe in the generally accepted clinical sense; it must be partially or fully effaced; and there must be no gross cephalopelvic disproportion. We believe that the cervix which points posteriorly is more difficult to dilate than one which is in the axis of the vagina and is filled out by the presenting vertex. Artificial rupture of the membranes facilitates the induction provided the aforementioned criteria are satisfied. In most cases, after spontaneous rupture of the membranes at term takes place, labor begins shortly, while in a few there is delay. One report indicates that 60 per cent of patients begin labor within one hour after rupturing membranes, while 90 per cent begin within 24 hours. In these patients admitted to the hospital with ruptured membranes at term, and without uterine contractions, exhibition of intravenous Pituitrin results in early completion of labor. Of course, the shorter the interval between the rupture of membranes and onset of labor, the lower the incidence of amniotic infection and puerperal morbidity. We do not advocate induction with a floating vertex which cannot be treated by Müller's method.

In a recent issue of the *Journal of the American Medical Association,*[13] under "Queries and Minor Notes," a physician asked whether the elective induction of labor was considered good obstetrical practice. The reply states, "One must admit that if it were possible and safe, it would certainly be to the advantage of both patient and physician for the baby to be delivered at a reasonable hour. Perhaps in a few more years we will consider this normal practice and, until then, accept an attitude of tongue-in-cheek toward it, rather than one of lifted eyebrows."

The difficult group of cases for elective induction are those in which labor should be induced about four weeks before term, especially primiparous preeclamptic patients. In this group, the cervix is unprepared and success is not to be anticipated. In fact, there is danger of possible fetal damage by persistence or repeated attempts, and we believe Pituitrin is contraindicated. Of course, if one artificially ruptures the membranes in a properly selected case, and the induction of labor with Pituitrin is unsuccessful, another method of delivery must be found. Perhaps, in the future, sympathicolytic drugs may

be found which will facilitate dilatation of the cervix in these circumstances. While the drug, Dihydroergotamine-45, has been utilized in this country and abroad, our experience with this drug has not been promising.[14] In fact, at the present time, we believe that no pregnant patient should receive Dihydroergotamine Mehanesulfonate (D.H.E.-45), at least intravenously, because of a high incidence of fetal damage.

3. Cephalopelvic Disproportion.—In many cases of borderline cephalopelvic disproportion, one finds that the labor is desultory. One hopes for establishment of good uterine contractions so that a proper trial of labor may be observed. We believe that no patient has a really adequate trial of labor as long as the membranes are intact. By rupturing the membranes artificially, if they have not already ruptured spontaneously, and by the employment of intravenous Pituitrin for a few hours at most, an early decision as to the best method of delivery may be made. We believe that careful personal observation by the attending obstetrician himself is absolutely necessary so that he may interpret and judge the quality of labor and its rate of progress. With the onset of adequate uterine contractions, and if there is no progress made within one to two hours, an immediate cesarean section is indicated. It is gratifying to report that many such cases, which in the past surely would have had abdominal delivery, now go on to successful vaginal delivery when trial labor with Pituitrin, as advocated here, is employed.

We emphasize again the fact that the use of Pituitrin intravenously in such cases should be attempted only by obstetricians experienced in this use of Pituitrin. In every such case, x-ray pelvimetry for detection of bony disproportion must be utilized. If there is absolute contraction of the pelvic measurements, no oxytocic agent is advised. Even if the inlet is adequate, the midpelvic planes must be carefully studied. For the most part, however, our cases indicate that relative disproportion associated with uterine inertia and positional dystocia all contribute equally to lack of progress in labor. Those cases in which uterine inertia and soft tissue dystocia were the indications for the first cesarean section comprise the majority of cases in which an infant may be delivered successfully through the birth canal after the initial abdominal delivery. That this is true is attested by the increasing number of patients who are being delivered in some clinics by the vaginal route after being delivered abdominally for the first pregnancy at another hospital where the indication for cesarean section was cephalopelvic disproportion. While we do not approve of this method, it is merely mentioned in passing. Cosgrove[6] recently reported 18 cases of borderline cephalic disproportion with desultory uterine contractions and four vaginal deliveries. With reasonably satisfactory labor, the indication for radical intervention became clear-cut in a relatively short period of time. Theobald[2] considered it safe to employ the Pituitrin drip in cases of contracted pelvis when the vertex was not engaged. We take exception to this point of view.

The following case is cited to contrast the use of Pituitrin as recommended by use with the older conservative procedure of allowing nature to take its course.

G. R., a 29-year-old, gravida ii, para i, abortions 0, was admitted to Cumberland Hospital in active labor at 4:30 A.M. on Oct. 29, 1951. She had had moderate regular pains lasting 30 to 40 seconds at five- to six-minute intervals since 3 P.M. on Oct. 28, 1951. She gave a history of ruptured membranes since 5 P.M. on Oct. 27, 1951.

Examination at the time of admission revealed a large, full-term, gravid uterus with the infant in left occipitotransverse position and the fetal heart beating at 140 per minute, heard in the left lower quadrant. Rectal examination showed the vertex at −3 station and the cervix to be 3 cm. dilated. The pelvis was clinically ample. The prenatal record of

the patient was apparently uneventful. X-ray pelvimetry (Thoms), was interpreted as showing a gynecoid pelvis with the anteroposterior axis of the inlet, 11 cm., and transverse axis of the inlet, 13 cm. The posterior half of the inlet was spacious, the sacrosciatic notch ample, and the subpubic angle was gynecoid.

The patient progressed poorly in labor and at 2:30 P.M., ten hours after admission, the pains were of as poor quality as previously and the cervix was 5 cm. dilated; the vertex was at –2 station. At 3 P.M., an intravenous infusion of Pitocin, 1:3,000 dilution, at 30 drops per minute, was begun, and 50 mg. of Demerol were given intravenously. The contractions were of good quality at 3:30 P.M. At 3:45 P.M., 100 mg. of Demerol were added to the Pitocin solution and the labor progressed satisfactorily so that at 4 P.M. the patient's cervix was fully dilated. At 4:30 P.M. she delivered spontaneously a 9 pound, 15 ounce infant in good condition from the right occipitoanterior position with a left mediolateral episiotomy. Her postpartum course was uneventful.

This patient's first admission to the hospital for labor was on Aug. 18, 1947. She was a primigravida, admitted at term at 11:30 P.M. in early labor, with pains at ten-minute intervals. These had started eight hours prior to admission. The prenatal course was uneventful and the maternal weight gain, 21 pounds. Abdominal examination disclosed a full-term fetus in the left occipitoanterior position and the fetal heart in the left lower quadrant beating at a rate of 140 per minute. Rectal examination revealed an effaced cervix, 2 cm. dilated with the vertex at –2 station. She was given an enema and the pains gradually became irregular and ceased. X-ray pelvimetry was requested and performed.

In the afternoon of Aug. 19, 1947, contractions lasting 30 seconds were observed at ten-minute intervals. The patient's labor continued with contractions occurring irregularly while she received fluids and sedation. Periods of rest alternated with periods of labor. On Aug. 21, 1947, the cervix was dilated to 5 to 6 cm. with the vertex still above the spine and at 12:30 P.M. the membranes ruptured spontaneously. At 1:30 P.M. the fetal heartbeat was of good quality and the vertex at –1 station. At 8 P.M., with the membranes now ruptured for eight hours and with the poor labor continuing, vaginal examination showed no evidence of disproportion. The fetal heartbeat was now absent. At 11:30 P.M., the patient had a chill while receiving intravenous fluids and the dosage of the antibiotic was increased. The following day, Aug. 22, 1947, at 8 A.M., the cervix was 9 cm. dilated and the vertex was at the spine, and weak pains occurred every four minutes. Three hours later the pains, at three-minute intervals, were still weak with the vertex at +2 station. She was delivered from the left occipitoanterior position of a stillborn infant weighing 8 pounds, 4 ounces, with the use of low midforceps with a right mediolateral episiotomy. Though the patient was treated with penicillin and sulfadiazine, she experienced a morbid postpartum course, the temperature reaching 102° F. on the third day, 100° on the fourth day, and 99.4° on the sixth day. She was discharged on the eighth day in good condition. Postmortem findings on the infant showed congenital pulmonary atelectasis and visceral congestion with hemorrhage into lung and spleen.

This case reveals quite clearly the difference between our present-day active management of uterine inertia contrasted with the old method of watchful waiting. We believe that the inactive treatment in these cases can result only in protracted labors with high maternal morbidity and fetal mortality, with an increase in operative deliveries.

4. Breech Presentation.—In breech presentation, we have successfully administered Pituitrin as described in this study. Evaluation of the size of the fetus by x-ray is not reliable, in our experience, but the pelvis may be accurately measured. Since the trial of labor with a breech presentation is after full dilatation and with delivery of the vertex, an early decision must be made as to the best route of delivery. With a fetus of average size and an adequate pelvis, we have not hesitated to stimulate labor by means of intravenous Pituitrin. It is especially helpful in shortening labor and establishing

rhythmic, forceful, effective contractions which are frequently not present, particularly in primiparas. In addition, there must be no x-ray evidence of a contracted pelvis. When the patient is admitted with ruptured membranes, after careful vaginal examination, stimulation of labor with Pituitrin is permissible. We have been impressed repeatedly by the eutotic type of labor with breech presentation initiated by Pituitrin.

5. *Parity.*—The incidence of spontaneous rupture of the pregnant uterus increased with parity. This fact leads us to limit the employment of Pituitrin to women who have borne not more than three children, but on occasion one might administer intravenous Pituitrin to a para iv. It is increasingly dangerous if the fetus is large. With babies over 9 pounds, relative cephalopelvic disproportion and positional dystocia may complicate the picture so that extreme caution is necessary. This is indicated by the increasing number of multiparous patients coming to cesarean section and those with difficult operative vaginal delivery. This is in spite of the fact that two or three other children may have been born successfully by the vaginal route.

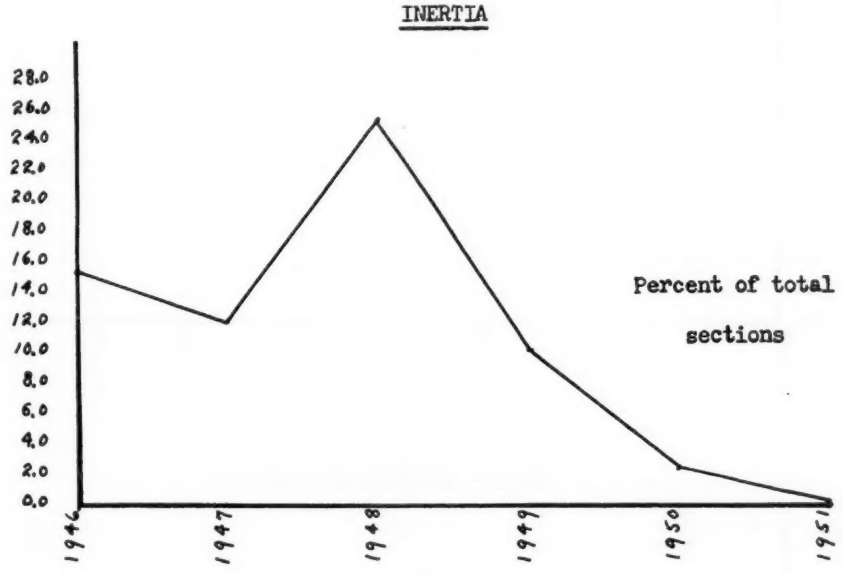

Fig. 1.

6. *Age.*—The elderly primigravid woman who is subject to an increased incidence of inertia and operative deliveries, may have labor stimulated by intravenous Pituitrin. Ideally, each primipara should have x-ray pelvimetry; certainly, primiparas over 35 years of age must have proper pelvic mensuration. Provided no bony disproportion exists, successful vaginal deliveries may be accomplished by a wider employment of intravenous Pituitrin in order to stimulate the inertia-type of labor so often encountered in these patients. The incidence of normal vaginal deliveries may be increased and the number of abdominal sections materially decreased.

7. *Twins.*—With an overdistended uterus and the membranes intact, Pituitrin should not be used. After the membranes have ruptured and a considerable quantity of amniotic fluid drained away, it is permissible to begin the oxytocic drip. Of course, there must be no abnormal presentation as verified first by vaginal examination. Our manner of delivering twins is to begin intravenous administration of Pituitrin slowly with the birth of the first baby.

After a short period of time, when uterine contractions have begun to be effective again, vaginal examination is performed to confirm the presentation and position of the second baby. With the vertex or breech presentation, the membranes are artificially ruptured and spontaneous delivery is awaited. An abnormal presentation is dealt with according to the best judgment at the time.

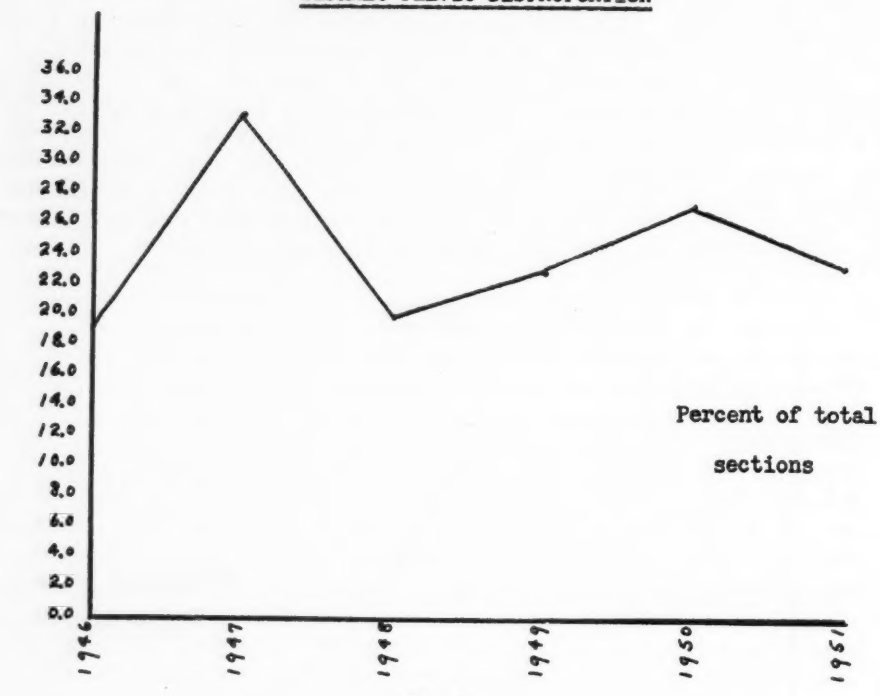

Fig. 2.

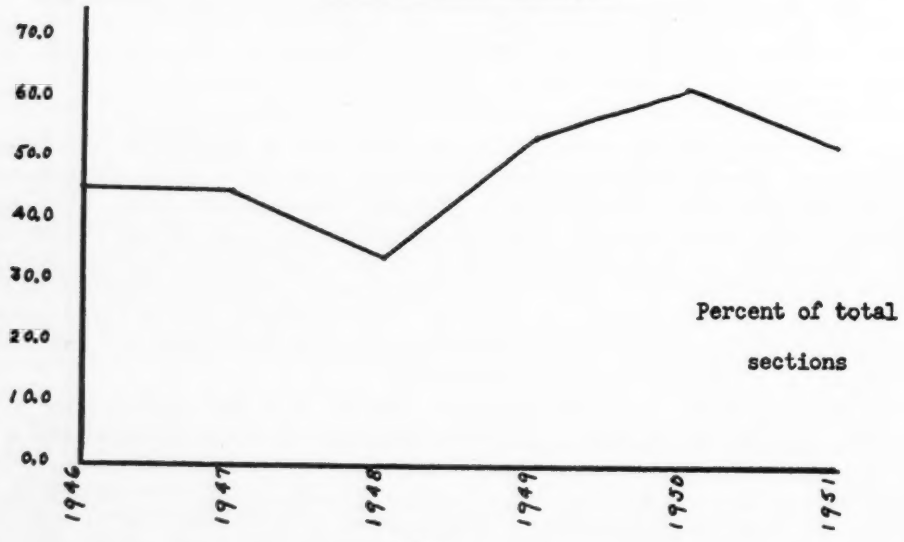

Fig. 3.

8. Large Fetus.—With the larger than average fetus, we do not hesitate to use Pituitrin so long as no disproportion exists. It goes without saying that the bony pelvis must be adequate and that presentation be normal.

9. Fetal Condition.—While the fetus must be in good condition before Pituitrin is begun, there exist a certain number of cases where we suspect fetal embarrassment to a degree. If, in a vertex presentation, there is passage

TABLE III.
Cesarean Section Rate

	PERCENTAGE
1946	2.65
1947	2.30
1948	2.35
1949	2.49
1950	2.45
1951	2.33

Cesarean Section Study

	TOTAL DELIVERIES	TOTAL SECTIONS	INERTIA	CEPHALOPELVIC DISPROPORTION	PREVIOUS CESAREAN SECTION	PLACENTA PREVIA	PARTIAL SEPARATION OF PLACENTA	ECLAMPSIA	OTHER
1946	979	26	4	5	12	1	2	1	1
1947	1,433	33	4	11	15	3	–	–	1
1948	1,485	35	9	7	12	5	1	–	1
1949	1,566	39	4	9	21	3	–	1	1
1950	1,627	40	1	11	25	3	–	–	–
1951	1,459	34	–	8	18	5	–	–	3

TABLE IV.

	PERCENTAGE OF TOTAL DELIVERIES	PERCENTAGE OF TOTAL SECTIONS
Inertia.—		
1946	0.40	15.4
1947	0.27	12.1
1948	0.61	25.7
1949	0.25	10.2
1950	0.06	2.5
1951	0.00	0.00
Cephalopelvic Disproportion.—		
1946	0.51	19.2
1947	0.76	33.3
1948	0.47	20.0
1949	0.57	23.0
1950	0.67	27.5
1951	0.54	23.5
Repeat Cesarean Section.—		
1946	1.22	46.1
1947	1.04	45.4
1948	0.80	34.3
1949	1.34	53.8
1950	1.53	62.5
1951	1.23	52.9

of meconium, one hopes for a relatively early termination of labor. Pituitrin will shorten these labors successfully. Of course, if the fetus is not born alive, we must not condemn the oxytocic unjustly. Perhaps the fetus would have succumbed from whatever cause initiated the fetal distress in the absence of the added oxytocic agent. There does not seem to be any added hazard for the fetus by shortening the interval from the time of appearance of meconium-stained amniotic fluid to expulsion.

10. Fetal Death.—With a dead fetus, there is no contraindication to the employment of Pituitrin. In two recent cases of missed abortion, intravenous administration of an oxytocic resulted in prompt evacuation of the uterine contents. One patient was initially primed with large doses of estrogen, whereas the second was bleeding mildly on admission and received no estrogen.

11. Premature Separation of the Placenta.—If one anticipates vaginal delivery and chooses to treat premature separation of the normally implanted placenta by amniotomy, the dilute Pitocin drip is advocated as being effective for stimulation or initiation of labor. If, after a short trial, progress is not observed, another method of delivery should be planned.

12. Marginal Placenta Previa.—In marginal placenta previa, especially in the multiparous woman, when planning for a vaginal delivery, one may rupture the membranes and attempt to induce labor by means of intravenous Pituitrin.

Postpartum Bleeding.—It is frequently mentioned, when intravenous Pituitrin is used for the induction of labor, or for uterine inertia, that there is an increase in postpartum bleeding in the third stage from uterine atony. When such bleeding occurs, we do not believe that the intravenous drip in the dilution mentioned is effective as an oxytocic substance. A stronger concentration of the agent is necessary for sustained uterine contraction, but Pituitrin does not seem to be as effective as Ergotrate.

That the judicious employment of Pituitrin is decreasing the incidence of operative vaginal deliveries and cesarean section is quite apparent. Even though there is an increasing incidence of cesarean section for bleeding in the last trimester of pregnancy, pre-eclampsia, diabetes, and other indications, the incidence of relative disproportion and uterine inertia is decreasing in our hands. This is shown in Figs. 1, 2, and 3, and Tables III and IV.

Summary

We must stress over and over again that Pituitrin by intravenous drip is not advocated for general use by untrained individuals. It is only for trained and experienced obstetrical specialists that the horizon has broadened. This agent is not a pancea for all obstetrical difficulties in labor but another invaluable and controllable agent which serves to decrease operative deliveries, stillbirths, neonatal deaths, and maternal morbidity in indicated cases. However, if its effectiveness is not evident quite clearly and distinctly after a few hours, another method of delivery should be promptly instituted. Persistence in its administration may lead to disaster and result in an unjust condemnation of the agent which was improperly employed.

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THE EPITHELIAL CHANGES IN THE FETAL CERVIX, INCLUDING THE ROLE OF THE "RESERVE CELL"*

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RECENTLY, two concepts regarding carcinoma of the cervix have gained credence.

1. The disease is of long duration and the invasive stage, so frequently seen clinically, is but a terminal phase of the illness.

2. There are certain changes which take place in the cervices of some pregnant women which resemble intraepithelial carcinoma, but which are reversible.

Gardner[1] has stated that in order to produce carcinoma of the genital tract in experimental animals three prerequisites are necessary: namely, a proper genetic strain, hormonal imbalance, and a trigger mechanism. It seems probable that in those pregnant women who exhibit reversible preinvasive carcinoma of the cervix, the proper genetic strain and hormonal imbalance are present, but the final trigger mechanism which converts this lesion into true carcinoma is absent. The validity of this hypothesis could be tested if a group of individuals could be found in whom the first two criteria were satisfied but who never had been subjected to the trigger mechanism and in whom carcinoma of the cervix was virtually unknown. It is fortunate that nature has provided us with just such an experiment. The fetus is subjected to the same hormonal influences as the mother without the possible occurrence of either the trigger mechanism or carcinoma. If enough fetal cervices were to be examined microscopically, in a certain percentage, changes similar to intraepithelial carcinoma should be seen, if the original hypothesis is valid. With this thought in mind, it was deemed worth while to study the cervices of newborn infants. The results of this investigation are, in part, presented here.

Material

Eighty-one uteri were examined, 80 of which were fetal or neonatal and one of which was from a girl 5 years of age who had died from pneumonia. The body weights of 55 fetuses were known; 32 were between 1,000 and 2,499 grams, while 11 were over 2,500 grams. The time of death was available in 61 of these cases. Seventeen were stillborn, 23 died on the first day, 14 lived from 1 to 4 days, and 7 survived from 4 days to 4 weeks.

This material was collected over a number of years and there was, therefore, little opportunity for gross study of the specimens. However, the gross anatomy of the fetal uterus is well known. Its shape differs markedly from that of the adult. By far the greatest portion is made up of the bulbar cervix

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which comprises two-thirds to five-sixths of the total length of the uterus. The small corpus which measures about one-half the diameter of the cervix is perched on top of this large organ.

There are two phases in the growth of the uterus during prenatal life.[2] Until the seventh lunar month the organ shows a lineal increase in correlation with the body length of the fetus. At about the seventh month the uterus enters into a phase of augmented lineal growth, and at birth it reaches a length about one-third greater than would be expected if the earlier growth rate, in respect to body length, had been maintained. After birth the organ loses length until in about 2^2 or 3^3 weeks it assumes essentially the dimensions which would have obtained had the early rate of fetal growth continued. On a theoretical basis it has been suggested that the growth of the uterus in the later fetal months consists of a substrate of typical fetal growth plus a secondary growth increment which is probably due to an extra stimulus furnished by placental or possibly ovarian hormones.

The uterus does not become sensitive to hormonal stimulation until some time after the seventh month of fetal life.[3] Frank[3] has stated that the placental hormone is the one involved, for he was able to demonstrate hyperplasia of the uterus due to extracts from this organ in experimental animals. In 1944, Moore[4] wrote that the hormones in the blood of the mother are of small molecular size and cross the placenta to act on the sensitive tissues of the fetus. This author felt that the most important hormone involved was estrogen. Chorionic gonadotrophin has been demonstrated in the tissues and fluids of the human fetus in about one-tenth the concentration found in the mother.[5] It has been suggested that the route by which these hormones reach the fetus is not transplacental but by filtration through the membranes. Although the quantity of this hormone found in the fetus is relatively small, it is still held to be physiologically significant.

The interstitial cells of the fetal testes are endocrinologically labile before birth.[6, 7] More recent observations show that the testes of fetal rats produce an androgenic hormone which stimulates the prenatal growth of the accessory sex organs.[8] However, similar activity of fetal ovaries has not been demonstrated. The developing female gonads probably do not produce female sex hormones, nor do they respond to injections of chorionic gonadotrophin.[8]

Scammon[2] stated that the reduction in the size of the fetal uterus after birth was due to hypoplasia and hypotrophy of the uterine muscle, together with a disappearance of the marked natal hyperemia of the organ. Hunter[9] confirmed these observations, and when graphs were prepared of the length of the two subdivisions of the uterus, namely, the body and the cervix, it was clearly seen that the increased fetal growth and the reduction in the length of the uterus after birth were concerned chiefly with the cervix. It follows quite naturally that the predominance of the cervix in perinatal life is reflected in cytologic changes in this organ as well. The endometrium of the fetal uterus is incompletely developed and relatively inactive. It generally shows only a small number of tubular glands, or perhaps a few wide invaginations of the surface epithelium. The lining epithelial cells show little evidence of secretion and the stroma is scant and compact. In contradistinction, the epithelial structures of the endocervix show a high degree of development and activity with glandular and epithelial hyperplasia and hypersecretion (Fig. 1). The changes which occur in the epithelium of the fetal cervix so clearly resemble those which take place in the maternal organ that differentiation of one from the other is often impossible.

The stratified squamous epithelium of the ectocervix of the fetus does not often extend into the external os. On the other hand, occasionally it is incom-

pletely formed and does not entirely cover the portio vaginalis of the cervix. The usual structure of this epithelium is a highly stratified layer of cells, closely resembling those of the maternal cervix. The basal cells are small with dark-staining nuclei somewhat elongated and occupying most of the cell. They are generally arranged in a layer two to three cells thick with abrupt transition into the large, squamous, mucified cells which form the greatest part of the epithelium. As in the adult when there is an increase in the number of layers of basal cells the term basal-cell hyperactivity was employed.

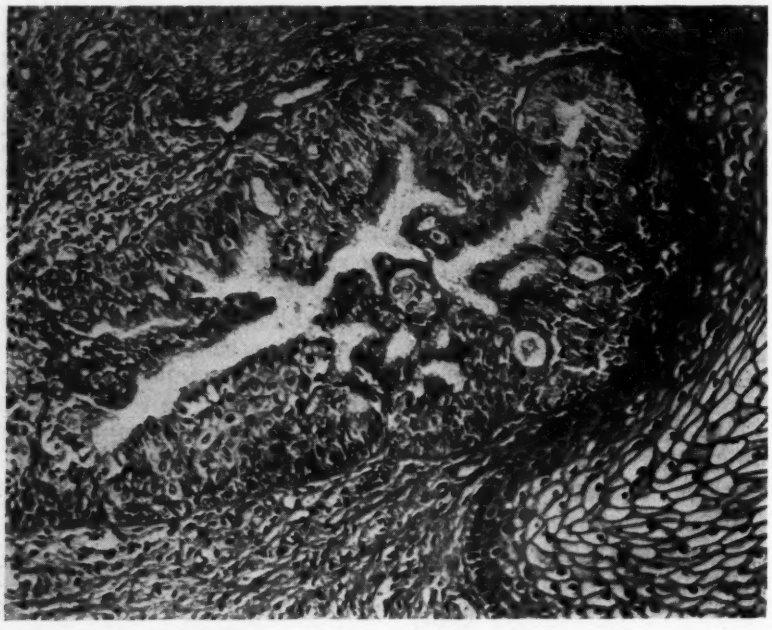

Fig. 1.—Cervix from a stillborn infant of 28 weeks' gestation showing hyperactive glandular epithelium.

In this study the endocervical and glandular epithelia show changes similar to those recently described for the cervix of pregnancy.[10] These comprise four basic phenomena, as follows:

1. Glandular hyperplasia—an increase in the number of glands.
2. Glandular epithelial hyperplasia—an increase in the number of cells lining the glands.
3. Adenomatous hyperplasia—the formation of multiple small gland spaces within the larger glands.
4. Epidermization—the presence of stratified squamous epithelium beneath the columnar epithelium or replacing it.

In the fetus, however, the latter two of these changes seem to be related to the "reserve cell" and to its increased activity. This cell is prominent in the fetal cervix. It is a primitive cuboidal or polygonal cell beneath the columnar epithelium of the cervix and has been noted previously by several investigators.[11, 12, 13, 14, 15, 16] According to Robert Meyer[16] who observed the presence of these cells, they are basal cells of fully differentiated squamous epithelium which remain after profuse endocervical secretion has macerated and caused desquamation of the more superficial layers of the squamous epithelium. This area is then replaced by actively growing columnar epithelium from adjacnt areas. When such basal cells are in direct contact with squamous epithelium of the ectocervix Meyer regards them as ingrowths.

This theory of development is disputed by Carmichael and Jeafferson[12, 13] who found large colonies of these cells high in the cervical canal and deep in the cervical glands. They reported that in 200 specimens "reserve cells" could be identified in 95 per cent of the cases. Despite the fact that these authors regarded these cells as undifferentiated remnants from the primitive lining of the genital tract they termed them "basal cells," which tends to suggest their origin from the basal cells of the mature squamous epithelium of the ectocervix. Others[14] have named them endocervical basal cells. However, the embryonic origin and growth potentialities are better indicated by the name "reserve cells." Howard, Erickson, and Stoddard[15] were the first to use this term in reference to the cervix, although it has been previously employed for other organs.[17] In a careful study of 400 adult cervices they were able to demonstrate quite clearly the histogenesis of squamous metaplasia from the "reserve cell." In 7 of their cases where squamous metaplasia showed atypism there was a resemblance to intraepithelial carcinoma. These authors contend that at least one type of intraepithelial carcinoma arises from the "reserve cell." Pund and Auerbach[14] had previously intimated that the "reserve cell" might be a frequent source of preinvasive carcinoma.

As stated above the "reserve cell" plays a prominent role in the morphological changes of the fetal endocervix. In 80 fetal and neonatal uteri the reserve cell was noted beneath the endocervical epithelium in 84 per cent of the cases and beneath the glandular epithelium in 69 per cent. Hyperplasia of the "reserve cell" occurred in about 20 to 30 per cent of the specimens in which these cells were identified (Table I). "Reserve cells" have been found in cervical glands in all regions and at all areas beneath the lining epithelium of the canal. The most common sites are the endocervix and the cervical glands near the squamocolumnar junction. They have been identified in both premature and mature fetuses as isolated cells or in single or multiple rows or in small clusters (Fig. 2).

TABLE I. DISTRIBUTION OF THE "RESERVE CELL"

	SLIGHT		MODERATE		MARKED		
	WITHOUT HYPERPL.	WITH HYPERPL.	WITHOUT HYPERPL.	WITH HYPERPL.	WITHOUT HYPERPL.	WITH HYPERPL.	NONE
Endocervical epithelium	37	4	10	11	0	5	13
Glandular epithelium	28	6	11	5	4	1	25

From the accompanying photomicrographs the "reserve cells" must be considered multipotential. They can reproduce themselves forming multilayers as shown in Fig. 3. This figure also shows the same cells forming columnar epithelium and stratified squamous epithelium. As they become more active they can form new glands (Fig. 1). With increasing hyperactivity, the configuration and arrangement of the cells become less regular and the nuclei take on irregular staining characteristics as shown in Figs. 4 and 5.

Epidermization was found in 24 specimens. Great difficulty, however, was encountered in understanding the pathogenesis of this change. In the light of the multipotential characteristics of the "reserve cell" it would seem logical to suppose that stratified squamous epithelium in the ectocervix, in juxtaposition to the squamocolumnar junction, or in the region of this junction, could be occasioned by a downgrowth of the epithelium of the ectocervix while more remote areas could arise from metaplastic "reserve cells." Mere juxtaposition, however, is no proof of this deduction, and on close examination of Figs. 6 and 7, the staining characteristics of the stratified epithelium

Fig. 2.

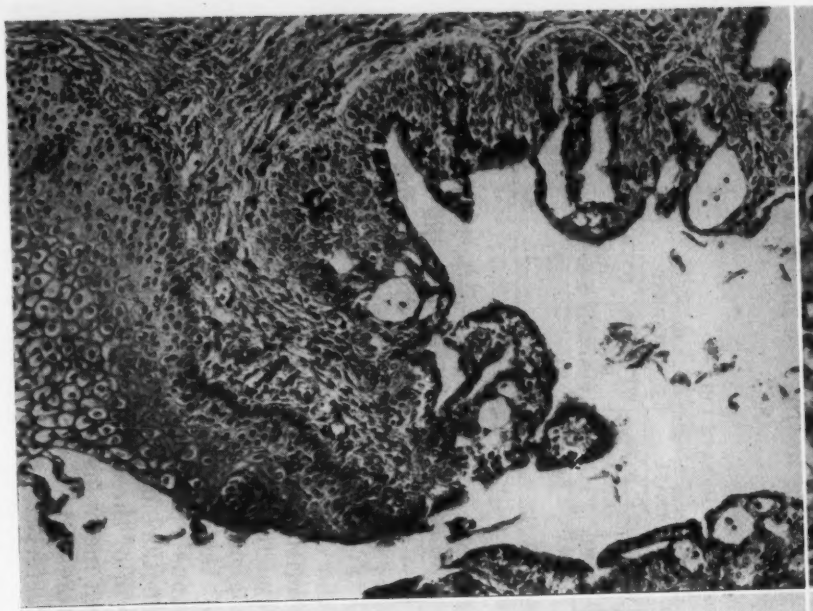

Fig. 3.

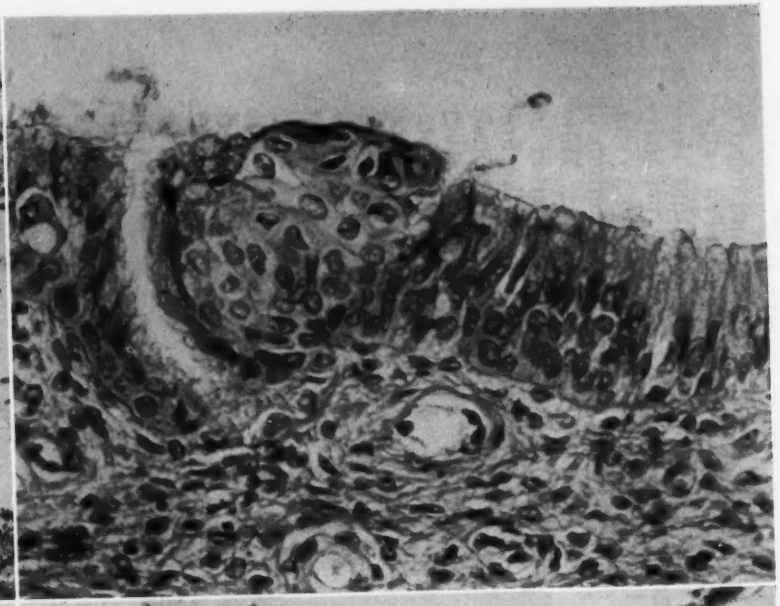

Fig. 4.

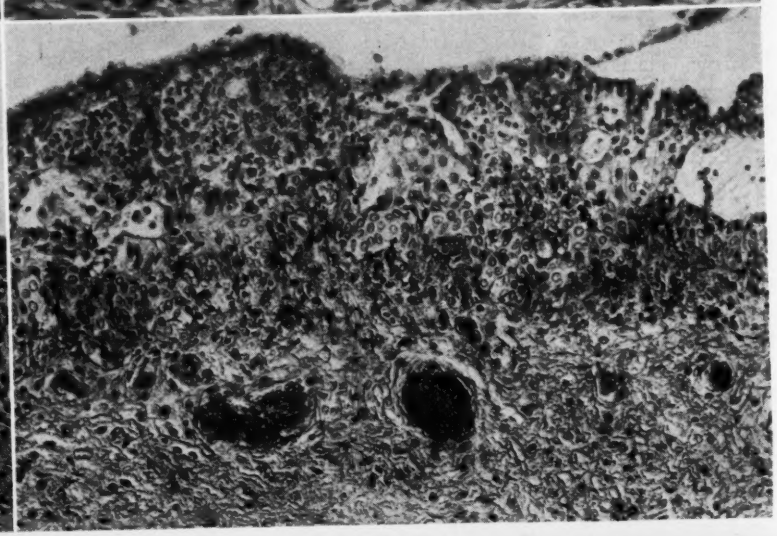

Fig. 5.

Fig. 2.—Cervix from a 2-week-old infant showing "reserve cells" beneath the endocervical epithelium.

Fig. 6.

Fig. 7.

Fig. 4.

Fig. 5.

Fig. 2.—Cervix from a 2-week-old infant showing "reserve cells" beneath the endocervical epithelium.

Fig. 6.

Fig. 7.

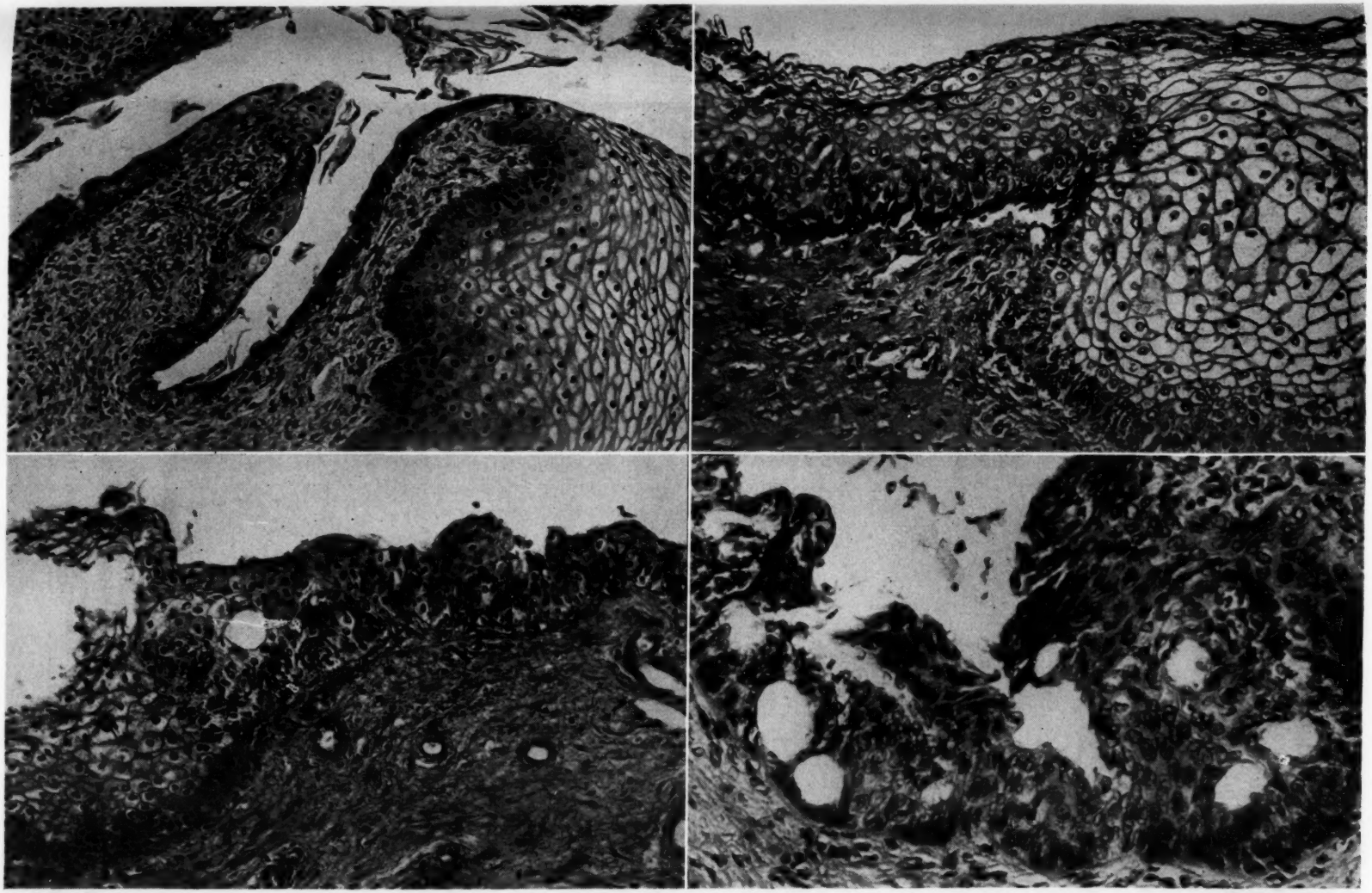

Fig. 8.

Fig. 9.

Figs. 6 and 7.—Epidermization in the cervix of two 1-day-old premature infants.
Fig 8.—Epidermization of "reserve-cell" origin in a term stillborn infant.
Fig. 9.—Epidermization of basal-cell origin with stratified surface epithelial overgrowth. Term fetus.

in the canal, even though it be continuous with the epithelium of the ectocervix are seen to differ from it. The cells are more basophilic and there is less mucification. Furthermore, close examination of the basal cells in some areas shows rather large, rounded, vesicular nuclei, more nearly resembling those of the "reserve cells." As one examines further specimens typified by Figs. 8 and 9 it can be seen that in most instances the squamocolumnar junc-

Fig. 10.

Fig. 11.

Fig. 10.—Basal-cell hyperactivity limited to the squamocolumnar junction. Three-day-old infant.

Fig. 11.—Generalized basal-cell hyperactivity in the ectocervix of a 3-week-old full-term infant.

tion remains clearly demarcated. The latter two figures show a basal layer of definite "reserve cells." They have undergone metaplasia to form stratified squamous epithelium but, in addition, they have retained their characteristic potentiality of forming new gland spaces. In the last figure there is marked irregularity of the hyperplastic basal cells. Close examination will show that this area has been overgrown by stratified squamous epithelium from the ectocervix and where the growth is most active the nuclei are hyperchromatic, irregular, and have lost their polarity. It is obvious that inasmuch as this is a cervix of a newborn child, intraepithelial carcinoma cannot exist and yet the resemblance is striking.

A summary of the changes found in the glands of the fetal cervix is shown in Table II.

TABLE II. GLANDULAR CHANGES

	SLIGHT	MODERATE	MARKED
Gland hyperplasia	11	22	5
Gland epithelial hyperplasia	17	23	5
Adenomatous hyperplasia	25	23	6

Basal-cell hyperactivity as characterized by an increase in the number and in the layers of the basal cells of the ectocervical epithelium was found in 17 specimens. In 7 it was limited to the squamocolumnar junction (Fig. 10), while in 10 it occurred in a generalized form through a large portion of the ectocervix (Fig. 11). As shown in Table III the ages of the fetuses in which the generalized form of basal-cell hyperactivity occurred were not always known. Therefore, this change should be disregarded for the hypotrophic phase may resemble it. However, in the 7 instances where basal-cell hyperactivity occurred at the squamocolumnar junction the fetuses were almost all in the perinatal period. While the change is not marked it is similar to that described in the adult. Hyperchromatism and mitotic figures are seen. No changes resembling intraepithelial carcinoma were discovered in the ectocervix.

TABLE III. BASAL-CELL HYPERACTIVITY

NO.	DEGREE	AGE	WEIGHT
	A. *Limited to the Squamocolumnar Junction*		
1	Slight	Newborn	
2	Slight	Newborn	
3	Slight		1,000-1,499 grams
4	Moderate	3 days	
5	Slight	5 days	
6	Slight	3 days	
7	Slight	4 weeks	
	B. *Generalized*		
1	Slight	1 day	
2	Slight	3 weeks	
3	Slight	3 weeks	
4	Slight	Unknown	
5	Slight	Unknown	
6	Moderate	9 days	1,000-1,499 grams
7	Moderate	Unknown	
8	Moderate	Stillborn	1,000 grams
9	Moderate	Unknown	
10	Moderate	5 years	

Summary

1. Changes similar to those seen in the cervix of the pregnant woman—namely, gland hyperplasia, gland epithelial hyperplasia, and adenomatous hyperplasia and epidermization, were found to be characteristic of the fetal cervix.

2. Adenomatous hyperplasia and epidermization seem to be related to activity of a multipotential cell termed the "reserve cell."

3. The "reserve cell" was capable of marked hyperplasia and metaplasia and occasionally exhibited disorderly growth characteristics somewhat similar to those shown in intraepithelial carcinoma.

4. Hyperactivity of the basal cells of the ectocervical epithelium was found in 7 instances at the squamocolumnar junction and, although not marked, resembled a similar change in the adult cervix.

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61 Eastern Parkway (Dr. Rosenthal)

Discussion

DR. HELLMAN.—As Dr. Rosenthal has indicated, his paper is a small but complete part of a much larger research problem dealing with epithelial changes in the cervix during periods of endocrine stress, such as fetal life, pregnancy, and senility. In reality it is aimed at the site of origin of carcinoma. There are at present three schools of thought on this subject: One which feels that carcinoma comes from hyperactive basal cells of the ectocervix, one that feels it may come from this area, or possibly from metaplasia in the glands, and the third that feels it has a field of origin near the squamocolumnar junction.

Studies such as Dr. Rosenthal's which indicate the tremendous potentialities of the "reserve cell" would seem to indicate that this cell may play a prominent part in the origin of carcinoma. If you will bear with me I would like to describe two aspects of the research now under way which deal with the "reserve cell."

The first case is that of a senile woman whose preoperative biopsy showed no activity of the epithelium of the endocervix. This patient received 150 mg. of stilbestrol a day for 2 weeks. The epithelium was hyperactive particularly as it related to the "reserve cell." There was also new gland formation beginning. In another case a peculiar hyperplasia of the "reserve cells" was discovered in a patient quite by accident. There was formation of new glands with sheets of atypical "reserve cells" adjacent to these. Whether this was a malignant or benign tumor, or whether it was actually tumor at all, I cannot say. Dr. Pund has such a patient in whom he was able to demonstrate the transition from "reserve cell" hyperplasia into malignant carcinoma of the cervix.

DR. CARL T. JAVERT.—I am a little bit at a loss to interpret these findings in the newborn infants referred to as fetuses. I think most of us think of fetuses as infants weighing 500 grams or maybe 700 grams. Most of these cases presented tonight are premature or full-term infants in the strict sense. A good many are stillborn infants perhaps. I am at a loss to correlate the picture in the cervix with any of the comments and references to carcinoma of the cervix. I think we should realize that this is an anatomical finding present in the newborn infants of a certain age. A good many of them were either stillborn or several days old. This study has a great many implications because all of us in the past have regarded so-called squamous metaplasia or the changes now referred to as the "reserve cell" of the cervix as the result of inflammation changes, such as endocervicitis, lesions following childbirth, etc. In that connection I would like to ask Dr. Rosenthal about the incidence of the "reserve cell" changes observed in the newborn infants.

DR. SAUL B. GUSBERG.—I was impressed with this very careful work of Dr. Rosenthal's. I have seen these changes but never understood them quite as clearly as I do now. But I also concur with Dr. Javert's belief, that probably these changes are not related to intraepithelial carcinoma. Certainly I don't think that this squamous metaplasia that we saw could be mistaken for intraepithelial carcinoma.

DR. J. EDWARD HALL.—I have been studying the fetal uterus since 1949, and by and large can confirm what Dr. Rosenthal has presented. However, there are many other phases which I think are very important and I think that Dr. Javert has mentioned one of them, that is, the inflammatory process which we see very frequently in the fetal cervix, even to the extent that we often find a real ulceration or ectopia of the cervix.

I would like to pose a question to Dr. Rosenthal, whether he thinks this so-called reserve cell is a totipotent cell of the stroma or whether it is something specific in this epithelial lining of the endocervix. I think this is a very important subject and may have a great deal of bearing on the etiological factor in carcinoma. I think very likely it must have occurred to Dr. Gusberg as it did to me, that the study of the intracellular enzymes in these cases might be most interesting. At least Dr. Hellman, in his study of adults, where he can get fresh tissue, might be able to produce slides that have been stained for intracellular enzymes to see the effects that his estrogen has had upon the cells. By and large, in the adult cervix we find no alkaline phosphatase, as we do in the endometrium, which is an indication of high estrogen content, and if he has produced these changes in the cervix with estrogen it would therefore seem that we might find some change in our intracellular enzymes. In the fetus of course we do not usually have our material in a fresh state which is necessary for the staining of enzymes.

DR. ROSENTHAL (Closing).—In regard to Dr. Javert's question as to the incidence of "reserve cells" and the changes in them, reserve cells were found in about 85 per cent of all the specimens examined, and in about 20 or 30 per cent of these specimens reserve cells showed hyperplasia. In a considerable number of these cases, in fact almost uniformly, where the reserve cell shows hyperplasia it also tends to show metaplasia into squamous cells.

In regard to epidermization or squamous metaplasia, this lesion was found in 24 of the 80 cases and some of the illustrative cases I have presented to you. I must disagree with Dr. Hall in regard to inflammatory changes in the cervix of the newborn infant, in that we have found little evidence of inflammation in the usual case. In fact, it seemed to us that this was a unique opportunity to study changes in a cervix devoid of inflammation, which is so constant a factor in the adult. It was seen occasionally in those infants who were several days or a couple of weeks old but in the stillborn infants and infants who died within a day or two, these inflammatory cells were generally not seen.

In regard to where the reserve cell comes from, and whether it comes from the stroma or not, I think the conception of Carmichael and Jaeffreson is the conception that we hold, namely, that they arise from the primitive lining of the genital canal, that they represent undifferentiated cells which remain. Apparently they remain all through the life of the female. As Dr. Hellman has indicated to you, they are found even in senile women and can undergo hyperplasia as the result of stimulation of large doses of estrogens.

I did not mean to indicate that I was showing you intraepithelial carcinoma in the cervix of the newborn infant. I do feel, however, that some of the changes that we see resemble it. Lee Howard and his colleagues at Duke University have traced the histogenesis of atypical squamous metaplasia from reserve cells right into intraepithelial carcinoma.

SPECIFIC HYPERTENSIVE DISEASE OF PREGNANCY: FACTORS AFFECTING INFANT MORTALITY*

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THE infant mortality remains high in pregnancies complicated by specific hypertensive disease, known as pre-eclampsia and eclampsia. The factors affecting this are either single or multiple. They chiefly consist of: (1) adequacy of prenatal care; (2) week of onset and duration and severity of specific hypertensive disease; (3) development of eclampsia; (4) onset of premature separation of the normally implanted placenta; (5) management of labor and delivery; (6) care of the premature liveborn baby.

Material

Incidence of Specific Hypertensive Disease.—This report includes the patients treated in the Obstetrical Department of Bellevue Hospital for 15 years ending May 31, 1950. Twenty-seven thousand twenty-eight patients were delivered during this time. Nine hundred thirty-nine had 1,010 pregnancies complicated by specific hypertensive disease, an incidence of 3.7 per cent.

Severity.—The severity of the hypertensive condition will be correlated with other factors affecting infant mortality. The severity was estimated when the patient was admitted to the hospital or shortly thereafter. It was measured from an analysis of the clinical subjective and objective findings.

Pre-eclampsia was considered severe when the patients showed two or more of the following symptoms: diastolic blood pressure readings above 110 mm. of mercury; two plus or more proteinuria; extensive generalized edema; fundus oculi changes consisting of edema, hemorrhage, or exudate; marked hyperreflexia; oliguria; and the subjective symptoms of threatening eclampsia.

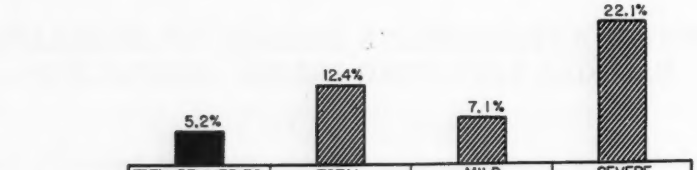
Infant Mortality.—The infant mortality is increased in pregnancies complicated by specific hypertensive disease. Fig. 1 shows that the loss was 5.2 per cent among the total delivered patients and 12.4 per cent in the hypertensives. The severity of the condition affected the infant's chance for survival. In the mild cases, the loss was only slightly higher than in the total delivered patients. The mortality was markedly influenced by the severe cases. Among these patients it was four times as great as in the nonhypertensive cases.

Factors Affecting Infant Mortality

Adequacy of Prenatal Care.—Prenatal care was considered inadequate if a patient did not return to the clinic regularly. Those who had no care were added to this group. The diet, economic status, and other general factors were not considered. Mild pre-eclamptic patients received ambulatory care in a special clinic. The obstetrical department of Bellevue Hospital is nonselective. Hypertensive patients were often admitted in active labor without having had any prenatal observation.

*Presented at a meeting of the New York Obstetrical Society, Jan. 8, 1952.

INFANT MORTALITY IN SPECIFIC HYPERTENSIVE DISEASE OF PREGNANCY

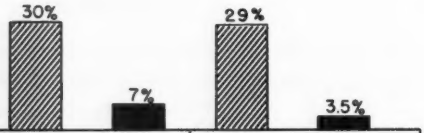


	TOTAL DELIVERIES 15 YEARS	TOTAL S.H.D.P.	MILD S.H.D.P.	SEVERE S.H.D.P.
NO. INFANTS	27,274*	1,040†	674	366
FETAL DEATHS	1,407	129	48	81

* INCLUDES 246 TWINS
+ INCLUDES 30 TWINS

Fig. 1.

EFFECT OF PRENATAL CARE ON THE INCIDENCE OF SEVERE PREECLAMPSIA AND ECLAMPSIA

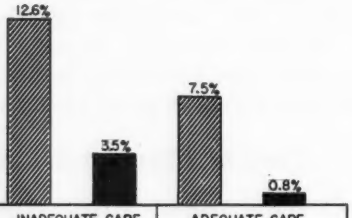


	INADEQUATE CARE	ADEQUATE CARE
NO. PATIENTS	528	482
SEVERE PREECLAMPSIA	159	140
ECLAMPSIA	37	17

▨ SEVERE PREECLAMPSIA
■ ECLAMPSIA

Fig. 2.

EFFECT OF PRENATAL CARE ON INFANT MORTALITY IN SPECIFIC HYPERTENSIVE DISEASE OF PREGNANCY



		INADEQUATE CARE	ADEQUATE CARE
NO. INFANTS*		538	502
FETAL DEATHS (129)	PREECLAMPSIA	68	38
	ECLAMPSIA	19	4

*INCLUDES TWINS
▨ PREECLAMPSIA
■ ECLAMPSIA

Fig. 3.

Fig. 2 demonstrates that prenatal care did not influence the incidence of severe pre-eclampsia. Thirty per cent of the cases became severe whether or not the patients attended the clinic. On the other hand, the occurrence of eclampsia was definitely affected. This condition developed twice as often in patients who did not avail themselves of clinic care.

Fig. 3 shows that regular clinic attendance had a favorable effect on the infant mortality. The infant loss was decidedly lower in pre-eclamptic patients with adequate attention. This was even more pronounced in the convulsive group.

Fig. 4 demonstrates that ambulatory pre-eclamptic patients developed a severe hypertensive state almost as readily as those patients without prenatal care. On the other hand, the infant mortality in the ambulatory patients was one-half that in the nonclinic group.

Forty-six pre-eclamptic patients refused to enter the hospital for treatment. Thirty-two and six-tenths per cent of their infants were lost.

EFFECT OF AMBULATORY CARE ON SEVERITY
OF SPECIFIC HYPERTENSIVE DISEASE OF PREGNANCY
AND INFANT MORTALITY

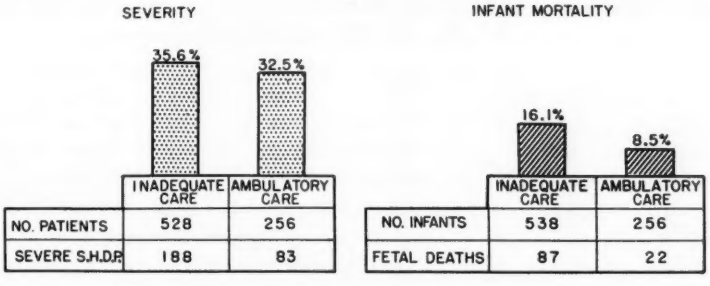


Fig. 4.

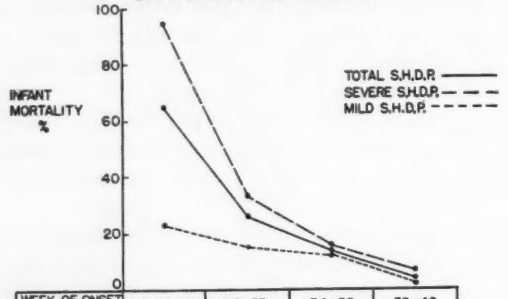
Time of Onset and Duration of Specific Hypertensive Disease.—Hospitalized antepartum pre-eclamptic patients were treated symptomatically. Pregnancy was generally allowed to continue until spontaneous labor set in. It was terminated if there developed: progression of the condition in spite of treatment; signs and symptoms of threatening eclampsia; and fundus oculi changes consisting of edema, hemorrhage, or exudate. On occasion, induction at term was used in controlled cases. The membranes were kept intact. If the induction failed, cesarean section was done only if the hypertensive state deteriorated or other obstetrical problems presented themselves.

The time of onset of the hypertensive condition affected the infant mortality. Fig. 5 shows that the infant loss was at its height in the early pregnancies. The deaths decreased when the condition began further along in gestation and reached their lowest point at term.

The infant's chance for survival was also influenced by the duration of the disease (Fig. 6). The deaths were at their lowest point when the hypertensive state was of short duration. They tended to increase in proportion to the length of time the condition lasted.

The methods of termination of pregnancy and infant mortality were analyzed in hospitalized antepartum patients. They were treated from 2 to 50 days prior to delivery. Seventeen patients with threatening eclampsia required delivery before two days. The pregnancies ended in one of three ways:

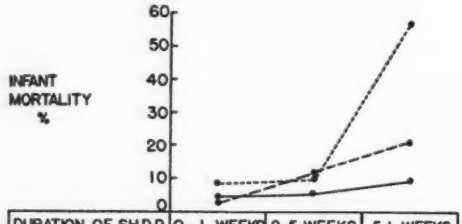
EFFECT OF TIME OF ONSET
OF SPECIFIC HYPERTENSIVE DISEASE OF PREGNANCY
ON INFANT MORTALITY



WEEK OF ONSET OF S.H.D.P.	UP TO 30	30-33	34-38	39-42
MILD S.H.D.P.	13	33	173	425
INFANT DEATHS	3	5	22	14
MORTALITY	23%	15%	12%	3.3%
SEVERE S.H.D.P.	19	58	122	149
INFANT DEATHS	18	19	21	11
MORTALITY	95%	33%	16%	7%
TOTAL S.H.D.P. MORTALITY	65%	26%	14%	4.4%

Fig. 5.

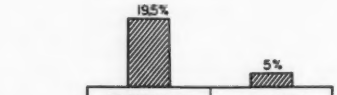
EFFECT OF DURATION OF SPECIFIC HYPERTENSIVE DISEASE
OF PREGNANCY ON INFANT MORTALITY IN CASES DELIVERED
AT 36, 38 AND 40 WEEKS



DURATION OF S.H.D.P.		0-1 WEEKS	2-5 WEEKS	5+ WEEKS
DELIVERED AT 36 WEEKS	NO. PATIENTS	58	29	7
	INFANT DEATHS	5	3	4
	INFANT MORTALITY	8.9%	10.3%	57%
DELIVERED AT 38 WEEKS	NO. PATIENTS	143	90	19
	INFANT DEATHS	5	10	4
	INFANT MORTALITY	3.5%	11.1%	21%
DELIVERED AT 40 WEEKS	NO. PATIENTS	314	152	31
	INFANT DEATHS	14	9	3
	INFANT MORTALITY	4.5%	5.9%	9.7%

Fig. 6

INFANT MORTALITY IN PATIENTS WITH SPECIFIC HYPERTENSIVE DISEASE
OF PREGNANCY HOSPITALIZED TWO OR MORE DAYS
(SPONTANEOUS ONSET OF LABOR)



	SEVERE S.H.D.P.	MILD S.H.D.P.
NO. INFANTS	82*	139+
INFANT DEATHS	16	7

* INCLUDES 3 TWIN PREGNANCIES
+ INCLUDES 3 TWIN PREGNANCIES

Fig. 7.

1. Fifty-two pregnancies were terminated because of threatening eclampsia, 20 by section and 32 by induction. Twenty-three of their 55 infants were lost. This was partly accounted for by 13 infants that were nonviable. The pregnancies were interrupted in order to lessen the hazards to the mothers and the viable infants.

2. Twelve successful inductions at term were carried out in mild controlled cases. All of these 14 infants lived.

3. Reports[1, 2, 3] are in agreement that the birth weight of a premature infant is the most important factor affecting the neonatal outcome. The interruption of pregnancy is frequently delayed in order to obtain increased weight of the infant. Diddle and Plass[4] point out: "Such a course frequently leads to intrauterine fetal deaths and thus defeats its own objective. Choice of intervention in such cases demands fine judgment for which no acceptable criteria are available."

The management of pre-eclamptic patients is often influenced by problems involving the fetus. These are: (1) Intrauterine deaths may occur suddenly. (2) Some infants do not increase in size as expected with time. (3) An inherent normal variation of infant weights exists in different patients at like periods of gestation. (4) Accurate estimation of fetal weight prior to delivery, especially in a premature, is often very difficult.

Two hundred fifteen pre-eclamptic patients were permitted to go into spontaneous labor. The infants were alive for at least two days after admission. Fig. 7 shows that the mild hypertensives can be carried along safely. The infant loss in these patients was not in excess of that found in the nonhypertensive group. On the other hand, it was four times as great in the severe hypertensives. The opportunities to reduce these deaths were more apparent than real. Sixteen infants were lost in the severe cases. Five were at term and probably could have been salvaged by interruption of the pregnancies. The remaining 11 presented problems involving estimation of fetal weight, method of termination of pregnancy, and the difficult decision of delivering premature infants which may not survive the neonatal period. This was proved in that 4 infants were nonviable and 7 weighed between 3½ and 5 pounds.

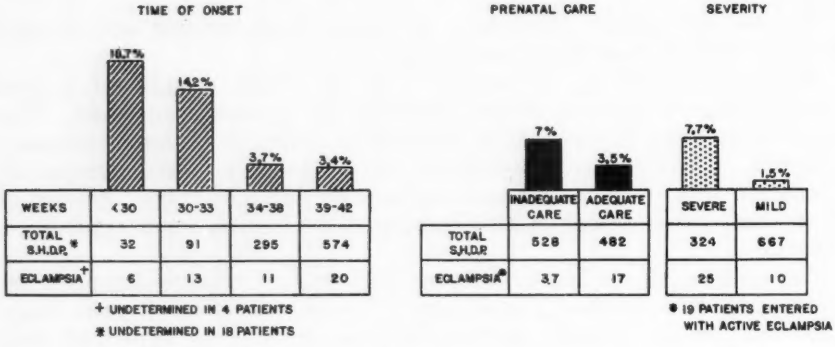
Development of Eclampsia.—There were 54 eclamptic patients in the specific hypertensive group. The majority were non-clinic patients who had active convulsive seizures prior to hospital admission or shortly thereafter. Fig. 8 shows that the incidence of eclampsia is much greater in the earlier weeks of gestation. The average occurrence was 4½ times more frequent up to the thirty-fourth week, as compared with the period from that point to term. The severity of the anteceding nonconvulsive state influenced the onset of eclampsia. In the severe cases of pre-eclampsia it developed 5 times more often than in the mild cases. The relation of prenatal care was described previously.

The development of convulsive seizures is a constant threat to the pre-eclamptic patient. Thirteen ambulatory nonconvulsive patients developed eclampsia. Six cases had become severe but the patients refused to be hospitalized. If these were excluded, the incidence was 3 per cent. This is significantly less frequent than the 7 per cent which manifested itself in patients without prenatal care.

The attack is usually milder if it occurs in a case treated in the hospital. Two hundred sixty-seven pre-eclamptics received such care for two or more days. Twelve developed eclampsia. Ten were mild intrapartum or postpartum cases. They had 14 infants. Three were lost.

The infant mortality increased precipitously when convulsions and/or coma supervened in a pregnancy complicated by pre-eclampsia. Fig. 9 shows that the infant loss was almost 40 per cent. This was 3½ times greater than in the nonconvulsive group. The type of eclampsia in relationship to labor

EFFECT OF TIME OF ONSET, PRENATAL CARE, AND SEVERITY OF PRECLAMPSIA ON THE INCIDENCE OF ECLAMPSIA



WEEKS	<30	30-33	34-38	39-42
TOTAL S.H.D.P.*	32	91	295	574
ECLAMPSIA+	6	13	11	20

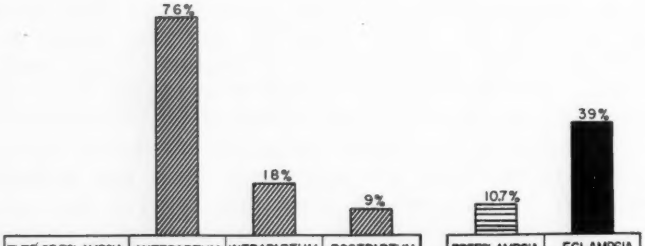
	INADEQUATE CARE	ADEQUATE CARE
TOTAL S.H.D.P.	528	482
ECLAMPSIA*	37	17

SEVERE	MILD
324	667
25	10

+ UNDETERMINED IN 4 PATIENTS
* UNDETERMINED IN 18 PATIENTS
* 19 PATIENTS ENTERED WITH ACTIVE ECLAMPSIA

Fig. 8.

INFANT MORTALITY IN PREECLAMPSIA AND ECLAMPSIA



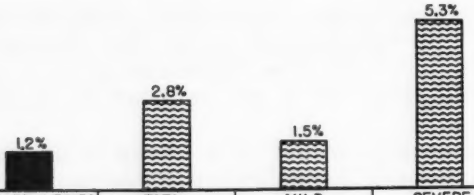
TYPE OF ECLAMPSIA	ANTEPARTUM	INTRAPARTUM	POSTPARTUM
NO. INFANTS	25*	11	22+
INFANT DEATHS	19	2	2

PREECLAMPSIA	ECLAMPSIA
982	58
106	23

* INCLUDES 1 TWIN
+ INCLUDES 3 TWINS

Fig. 9.

INCIDENCE OF PREMATURE SEPARATION OF PLACENTA IN SPECIFIC HYPERTENSIVE DISEASE OF PREGNANCY



	TOTAL DELIVERIES 15 YEARS	TOTAL S.H.D.P.	MILD S.H.D.P.	SEVERE S.H.D.P.
NO. PATIENTS	27,028	1,010	657	353
PREMATURE SEPARATION	326	29	10	19

Fig 10.

influenced the survival rate. Three-fourths of the patients with antepartum convulsions lost their infants. The lowest fatalities were in the postpartum group.

The infant loss was highest in those patients who did not avail themselves of adequate prenatal attention. Nineteen of the 23 deaths took place in these cases. The infant casualties in eclamptic mothers made up 17 per cent of the 129 that took place in all the specific hypertensives.

Premature Separation of the Placenta.—The cause of premature separation of the placenta cannot often be determined. Observers[5, 6, 7] are in accord that a large percentage have an associated hypertensive condition.

Fig. 10 shows that the incidence was not increased in the mild cases. In these patients its occurrence was almost identical with that in the nonhypertensive group. On the other hand, it developed 4½ times more often in the severe cases.

The infant deaths were exceptionally high; 26 of the 29 died. These deaths took place as follows: 20 before hospital admission; 3 in labor; 2 within 48 hours neonatally; and one died 2 days after the mother was admitted for antepartum observation.

Some interesting points were noted notwithstanding the small number of cases:

1. Twenty-one patients had inadequate prenatal care; 5 were receiving ambulatory treatment for mild pre-eclampsia.
2. Two of the 267 patients developed this condition while getting antepartum hospital attention for two or more days. One of these babies survived.
3. The 10 cesarean sections performed for this condition made up 15 per cent of those done in the hypertensive patients. Eight babies were dead prior to the operations.
4. The infant deaths produced 20 per cent of the 129 lost in the hypertensive patients.
5. Sixteen infants were premature. These made up 9 per cent of the 176 in the premature group.
6. Two cases developed in eclamptic patients. Both infants were lost.

Labor and Delivery.—Some infant deaths can be attributed to labor and delivery. Schreiber[8] states: "During labor, sedatives and inhalation anesthesia increase the incidence of asphyxia in direct proportion to the amounts given and duration, respectively."

A detailed analysis of the analgesics and anesthetics which were used is not included in this report. Some general principles were followed. They were: the administration of minimal amounts of analgesic drugs and the use of the low forceps and/or episiotomy[9] in premature births; pudendal procaine nerve block for vaginal delivery; and, finally, avoidance of inhalation anesthesia in cesarean section.

Table I shows that the cesarean sections performed in patients with specific hypertensive disease were more than double those done in the nonhypertensive group. This increase was chiefly accounted for by those done for premature separation of the placenta and threatening eclampsia. One convulsive patient had a section after she recovered from her seizure. Twenty were done primarily for pre-eclampsia, 10 for placental separation, and 8 for mixed indications which included the hypertensive condition. The remaining 25 were performed for the usual obstetrical complications.

The second stage of labor was shortened to prevent trauma to the premature infant and progression of the hypertensive state. The incidence of forceps delivery was double that in the total delivered patients.

TABLE I. INCIDENCE OF CESAREAN SECTION AND FORCEPS DELIVERY IN SPECIFIC HYPERTENSIVE DISEASE OF PREGNANCY

	TOTAL CASES 15 YEARS	CESAREAN SECTION		FORCEPS DELIVERY	
		NO. PATIENTS	% SECTIONS	NO. INFANTS	% FORCEPS
Total Deliveries	27,028	752	2.78	2,958*	10.8
S.H.D.P.	1,010	63	6.2	226†	21.7

*Includes 246 twins.
†Includes 30 twins.

Care of the Liveborn Infant.—Infants weighing less than 5 pounds were considered premature and those below 3 pounds nonviable. They were sent to the premature unit of the Pediatric Service. Heat and oxygen were administered before and in transport. The normal term infant was kept on the obstetrical service.

Fig. 11 shows that the incidence of prematurity was increased in pregnancies complicated by specific hypertensive disease. The rise was principally accounted for by the severely hypertensive patients. In this group it was almost three times as frequent as in the mild cases. On the other hand, in the latter group, it was identical with the nonhypertensive patients.

Fig. 12 demonstrates the principal causes of the premature births. The largest number resulted from spontaneous labor for unknown reasons. The rest of the premature births were brought about by artificial termination of pregnancies which were threatening to become eclamptic, twin births, and premature separation of the placenta.

One hundred eighteen premature infants were liveborn. Of these, 24 died in the neonatal period; 18 succumbed in the first 48 hours of life. The remainder died weeks later of usual pediatric complications.

The neonatal outcome of the premature infant was influenced by its weight. Although the cases were numerically small, Fig. 13 demonstrates an increased rate of survival with the greater weight of the infant.

Summary

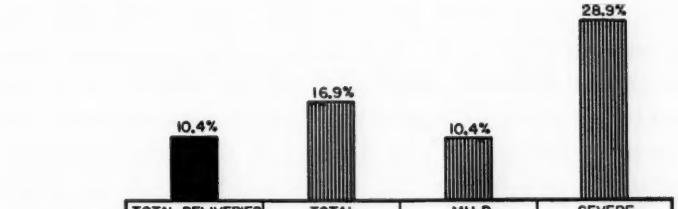
The infant mortality and factors affecting it were reviewed in 1,010 patients whose pregnancies were complicated by specific hypertensive disease (pre-eclampsia and eclampsia). These cases occurred among 27,028 delivered patients in Bellevue Hospital during a 15 year period ending May, 1950.

The severity of the hypertensive state of its own accord, and when correlated with other factors, influenced the infant deaths. The loss was four times as great in severe cases, and in mild ones only slightly above that in the nonhypertensive patients. The incidence of eclampsia, premature separation of the placenta, and prematurity was consistently higher in the severely hypertensive patients. These conditions, in turn, contributed to the infant loss.

The development of severe pre-eclampsia was independent of prenatal care. It occurred alike whether or not the patient attended the clinic. On the other hand, eclampsia ensued twice as often, and the infant mortality was decidedly greater, in patients who did not have adequate care.

The infant loss was affected by the time of onset and duration of the hypertensive state. The casualties were at their peak in the earlier weeks of gestation and with continuance of the condition.

INCIDENCE OF PREMATURITY
IN SPECIFIC HYPERTENSIVE DISEASE OF PREGNANCY



	TOTAL DELIVERIES 15 YEARS	TOTAL S.H.D.P.	MILD S.H.D.P.	SEVERE S.H.D.P.
NO. INFANTS	27,274	1,040	674	366
NO. PREMATURES	2,845	176	70	106

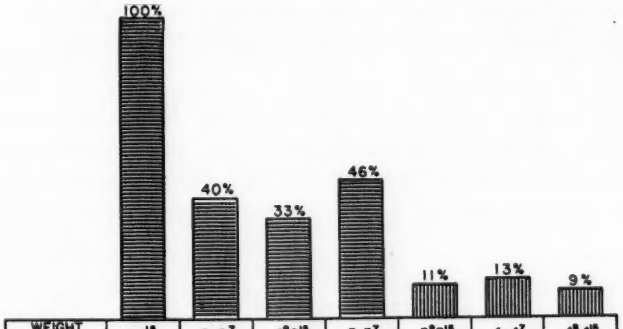
Fig. 11.

CAUSES OF PREMATURE DELIVERY
IN SPECIFIC HYPERTENSIVE DISEASE OF PREGNANCY
(176 INFANTS)

	UNKNOWN SPONTANEOUS LABOR	INDUCED LABOR OR CESAREAN SECTION	TWINS	PREMATURE SEPARATION OF PLACENTA
NO. INFANTS	115	26	19	16

Fig. 12.

NEONATAL MORTALITY OF PREMATURE INFANTS
IN SPECIFIC HYPERTENSIVE DISEASE OF PREGNANCY



WEIGHT LBS - OZS	$1\text{-}1^{15}$	$2\text{-}2^{7}$	$2^{8}2^{15}$	$3\text{-}3^{7}$	$3^{8}3^{15}$	$4\text{-}4^{7}$	$4^{8}4^{15}$
LIVE PREMATURES	4	5	6	13	18	38	34
NEONATAL DEATHS	4	2	2	6	2	5	3

Fig. 13.

Pregnancies were terminated to lessen the hazards to mother and infant when nonconvulsive patients developed signs and symptoms of threatening eclampsia. Patients with severe pre-eclampsia treated conservatively sustained an infant loss four times greater than those with mild cases. In the latter group it was identical with that in the nonhypertensive patients. Nonviable and premature infants contributed to the deaths in a large measure, both in the severe pre-eclamptics and in those threatened with eclampsia.

The incidence of eclampsia was highest in nonclinic patients, those with severe pre-eclampsia, and before the thirty-fourth week of pregnancy. The infant loss was 3½ times greater than in the pre-eclamptic group. This took place chiefly in the patients with antepartum convulsions. When eclampsia developed in a treated hypertensive patient it was usually a mild intra- or postpartum type.

The majority of the patients with premature separation of the placenta had not attended the clinic. Its incidence in mild cases was identical with that among the nonhypertensive patients. It was 4½ times more prevalent in the severe cases. Almost all the infants were lost.

The cesarean section rate in specific hypertensive disease was approximately 2½ times that of the total delivered patients. The increased operations were largely accounted for by those done for threatening eclampsia and premature separation of the placenta. The number of forceps deliveries was double that done in the nonhypertensive patients.

The incidence of prematurity was relatively high. It was not altered by the mild cases, where it was identical with the nonhypertensive cases. However, it was almost three times more prevalent in the severely hypertensive cases. Three-fourths of the neonatal deaths of premature infants occurred within the first 48 hours of life. The increased weight of the premature liveborn infants favorably influenced their chances for survival.

I am grateful to Dr. Gordon Jonas for his inestimable aid in the statistical phase of this paper.

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PAPILLOMA OF THE CERVIX

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PAPILLOMAS, including condyloma acuminatum, are rarely found on the cervix. There have been to date only twenty-three verified cases reported. The finding of eight additional cases of papilloma of the cervix has afforded the opportunity to focus more attention on these lesions by reviewing the literature and by reviving the discussion of the following controversial problems:

1. Definition
2. Relationship to condyloma acuminatum
3. Incidence in pregnant and nonpregnant states
4. Malignant potentialities

Ewing[1] defined a papilloma as a benign tumor of pavement epithelium with supporting tissue in normal arrangement. This definition excludes the benign tumors of columnar epithelium (adenomas), as well as those composed of both columnar and stratified squamous epithelium where replacement of the former by the latter is clearly evident, and epithelial growth consisting of hypertrophy and hyperplasia.

In agreeing with the concept that endocervical polyps with squamous metaplasia are not to be considered papillomas, Meyer[2] stated that, in addition to the microscopic picture, the location of the base of the growth would help to differentiate the two lesions. Unfortunately, however, three sets of circumstances tend to militate against any aid this might give. First, as a result of eversion and erosion adenomatous polyps may seem to arise from the exocervix; second, because of replacement of columnar epithelium by squamous epithelium, papillomas may arise in areas originally lined by columnar epithelium and consequently seem to originate from the endocervix; and, finally, some tumors have their base exactly astride the junction of the exocervix and the endocervix.

Marked thickening of the epithelium as a result of hypertrophy and hyperplasia have been included by some under the classification of papillomas. It may be that these variations are preliminary to the future development of papillomas, but epithelial changes consisting solely of hypertrophy and hyperplasia should not be classified as neoplasms.

Review of the Literature

In 1921 Wharton[3] presented three interesting cases of papillary lesions on the exocervix; one proved to be tuberculous in origin; the second an inflammatory process, there being no epithelium present; and the third a typical example of condyloma acuminatum.

The same year Meyer[2] reviewed the German literature and added several cases of his own. He accepted as a true papilloma a case previously presented by Kleeman, although the lesion did not have the hard quality which he felt should be present. Schultz's case likewise was acceptable but was considered to be condyloma acuminatum because the lesion was multiple. The tumor reported by Heitzman was acceptable as a papillomatous lesion although it showed invasive carcinoma at its base. Meyer then presented four cases of condyloma acuminatum, two in pregnancy and two with prolapse, the latter apparently resulting from irritation by pessaries. He presented one case of a papilloma in a 20-year-old virgin. This warty lesion was present at the junction of the exocervix and endocervix. Finally, he presented a papilloma which had changed subsequently to a low-grade malignant lesion.

In 1923, Mohnle[4] found a papillomatous lesion in the cervix of a 31-year-old woman during care for a septic abortion. Biopsy showed broad sheets of cells with nests growing into a gland-bearing area.

In 1927, Cattaneo[5] presented a small tumefaction growing on the surface of the cervix of a 50-year-old woman, which proved to be a typical papilloma microscopically. This was thought at the time to be malignant because there were nests of squamous cells in the glands.

In 1938, Mershon[6] reported two cases of solitary tumors of the cervix in pregnancy. Originally, both were thought to be malignant but opinion was later revised. Therapy consisted of radium in both instances and operative interruption of pregnancy in one (the other aborted spontaneously).

In 1940, Treite[7] discussed the whole problem of papillomas and presented two cases of condyloma acuminatum in pregnancy and one papilloma in a 34-year-old patient.

Six cases were reported by Edmondson and associates[8] in 1947. Of these, five patients were definitely pregnant and one probably was not. One of these cases had been reported previously by Mershon and one other consisted solely of hypertrophy and hyperplasia. Consequently only four of these cases can be considered new cases of papillomas.

In 1948, Susan and Meister,[9] at the delivery of an 18-year-old primigravida, noted a 1 cm. circular, white, edematous papule with multiple, minute, short, papillary projections on the surface of the cervix. The lesion was excised and revealed a typical papillomatous pattern.

In the course of two hundred biopsies taken at the time of delivery, Sheets[10] noted two cases of marked thickening of squamous epithelium which he considered condylomatous papillomas. These changes, however, appear to be examples of hypertrophy and hyperplasia, and are not true neoplasms.

In the same year Hill[11] biopsied a woman's cervix at 36 weeks' gestation because it was grossly hypertrophic and showed numerous areas of ulceration. The pathologists were equally divided as to whether the lesion was benign or malignant. There was marked proliferative activity in the endocervical and squamous portions of the cervix, particularly the latter. The squamous epithelium showed considerable downgrowth into a gland-bearing area and mitotic figures were present in large numbers. This lesion seems to be primarily hypertrophy metaplasia and hyperplasia and probably should not be considered a neoplasm.

In 1950, Wolfe[12] biopsied a tumefaction on the cervix of a 29-year-old woman who was six to eight weeks pregnant. This proved, microscopically, to be a typical papilloma. The lesion persisted throughout pregnancy, but disappeared fifteen weeks post partum.

In summary, 23 papillomas have been reported. Eight of these have been of the condylomatous variety, 13 have been of the noncondylomatous benign

type and 2 have been malignant. Twelve of the 23 patients were pregnant when the lesions were first discovered.

Case Reports

CASE 1.—S. C., was a 30-year-old Negro woman, gravida ii, para ii, with a negative Frei test, Wassermann four plus, and not pregnant. She was seen on Dec. 19, 1950, at Kings County Hospital with a chief complaint of vaginal discharge. On physical examination there were many small skin tabs noted, 3 to 5 mm. in diameter, soft, sessile, pedunculated, and solitary, present since childhood. The greatest number were in the region of the buttocks. One was removed for microscopic study and was reported as a benign papilloma. Pelvic examination revealed the absence of condylomata acuminata on the perineum, vulva, and vagina. The cervix was anterior and long. There was a large cauliflower-like mass extruding from the cervical os, which was bleeding actively. The uterus was the size of a 10 to 12 weeks' gestation. Initial therapy of the cervical lesion was topical application of podophyllin. This apparently failed as the lesion continued to grow.

In 1945 she had had a tubovarian abscess drained abdominally. She had been seen again in 1947 with a chief complaint of discharge. On Feb. 19, 1950, she had been admitted to the Brooklyn Cancer Institute with the same complaint and at this time a cervical biopsy was taken and reported as chronic cervicitis. During these visits no neoplastic lesions were noted on the cervix.

She was admitted to Kings County Hospital on Dec. 24, 1950, for profuse bleeding. The cervix was 1 cm. dilated with a pedunculated mass extruding from the os. On Jan. 22, 1951, a total hysterectomy and bilateral salpingo-oophorectomy were performed, but the neoplasm was not completely extricated. On March 3, 1951, she was discharged to the outpatient department, only to be readmitted on March 21 for profuse bleeding per vaginam. At this time vaginal examination revealed a papillary lesion involving the upper third of the vagina. On April 6, 1951, radium was inserted into the vagina and a total dose of 1,000 mg. hr. applied. Following this, the bleeding ceased and she was discharged to the outpatient department. On Aug. 21, 1951, the vaginal vault was filled with a large papillary mass approximately 5 cm. in diameter. The abdominal wound had been draining continuously. Investigation revealed that this resulted from a fistulous trace connected to the sigmoid colon. A colostomy was performed on Sept. 19, 1951. At this time the cul-de-sac was filled completely with a friable papillary type of tumor extending to the brim of the pelvis. Since that time her condition has been slowly but steadily deteriorating.

On Dec. 19, 1950, a biopsy was taken of the papillary lesion on the cervix.

Microscopic:—Sections reveal a papillary structure composed of hypertrophic, hyperplastic, stratified squamous epithelium, the cells of which are quite regular. It is supported by a connective tissue framework which is moderately infiltrated with small mononuclear cells. The epithelium appears moderately active. All stages of normal mitotic figures are present. There are numerous polymorphonuclear leukocytes in the epithelium. No evidence of keratinization is noted.

Diagnosis.—Papilloma of the cervix consistent with condyloma acuminatum.

On Jan. 13, 1951, another biopsy was taken of the papillary lesion on the cervix.

Microscopic:—These sections differ from the former only in that there are piled up nuclei in the basal areas and some focal zones of keratinization on the surface.

Diagnosis:—Papilloma of the cervix consistent with condyloma acuminatum. (Figs. 1 and 2.)

On Jan. 22, 1951, a total hysterectomy and bilateral salpingo-oophorectomy were performed,

Gross:—Specimen consists of a uterus and two adnexal masses. The uterus measures 7 by 5 by 5 cm. The cervix is difficult to identify as such. It is covered by gray-white, firm papillations over the entire external surface and up the canal to the internal os. There are several papillations which seem to have extended 1 mm. beyond the internal os. On section these papillations appear to be on the surface. The uterine wall appears normal. The endo-

metrial cavity is lined by a pink membrane approximately 1 mm. in thickness. The adnexal masses measure 5 by 4 by 2 cm., and on neither side is the ovary identifiable and on only one side is the Fallopian tube recognizable.

Microscopic:—Papillary structures, similar to those previously noted, now are found in the body as well as on the surface of the cervix, in the endometrium, and in the myometrium. There is increased evidence of keratinization with pools of keratin and keratin-producing cells noted. The cells of the epithelium show increased evidence of malignancy. There is loss of polarity as well as considerable piling up of nuclei. There are mitotic figures and dyskeratotic cells present.

Fig. 1.

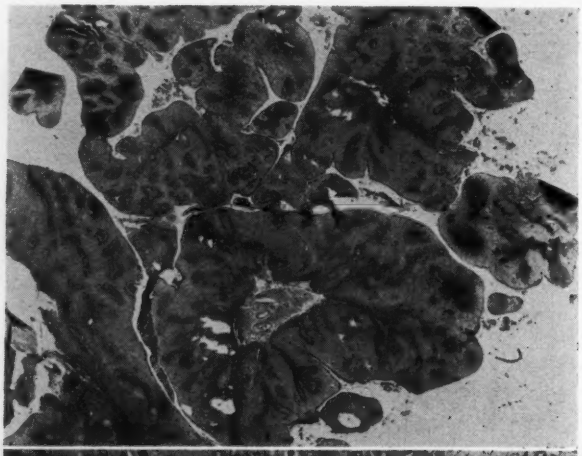

Fig. 2.

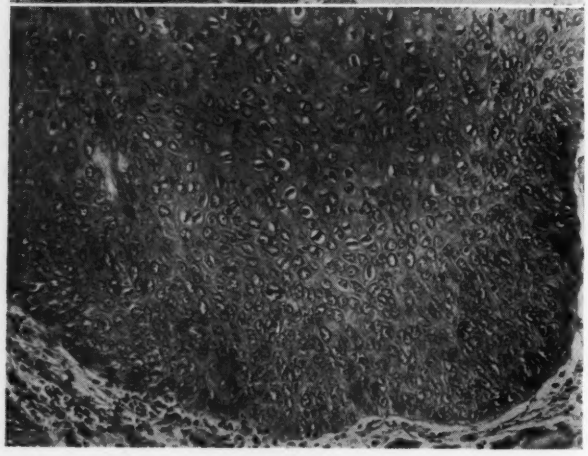

Fig. 1 (Case 1).—Note papillary structures with hypertrophic, stratified squamous epithelium. (×17.5.)

Fig. 2 (Case 1).—An occasional mitotic figure is present. Some piling up of nuclei is seen in the basal zone. However, the histologic picture points predominantly to a benign papilloma. (×200.)

Diagnosis:—Papillary epidermoid carcinoma of the cervix with local extension to the endometrium and myometrium (Fig. 3).

Endometrium, proliferative phase; acute and chronic salpingitis, bilateral; normal ovaries.

On Sept. 19, 1951, at the time of colostomy, a biopsy was taken of the papillary tumor tissue found in the cul-de-sac.

Microscopic:—The neoplasm has maintained its papillary structure. There is loss of polarity and piling up of nuclei. Some tendency to keratinization is noted.

Diagnosis:—Papillary epidermoid carcinoma (Fig. 4).

Final Diagnosis:—Papilloma of the cervix consistent with condyloma acuminatum with subsequent conversion to papillary epidermoid carcinoma of the cervix with invasion by direct extension to the endometrium. myometrium, and pelvic peritoneum.

Fig. 3.

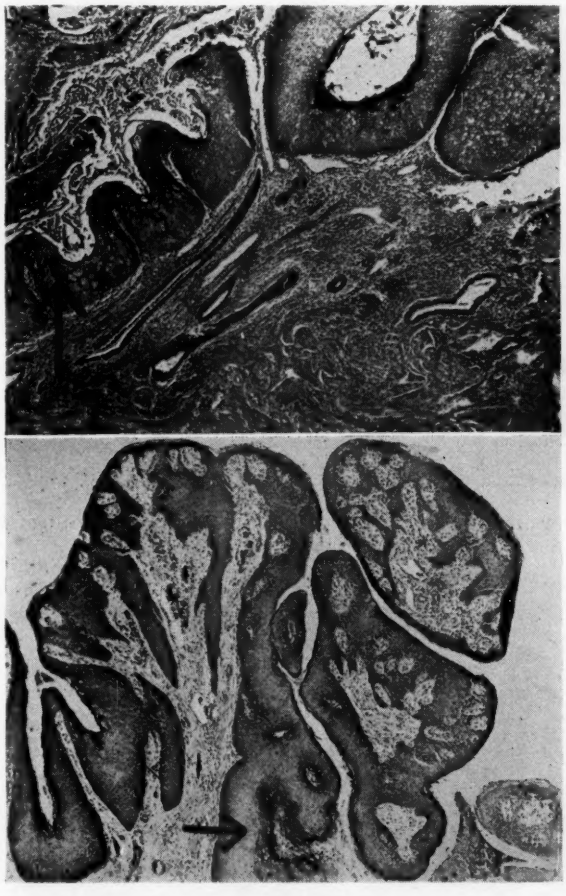

Fig. 4.

Fig. 3 (Case 1).—Hysterectomy specimen reveals definite evidence of invasion. Nests of squamous epithelium can be seen in the endometrium. There are pools of keratin noted in the convoluted nest at arrow. (×40.)

Fig. 4. (Case 1).—Specimen removed from peritoneal cavity at time of colostomy. Papillary architecture with hypertrophic squamous epithelium still retained; however, a definite granular layer is present on the surface, covered by a thin layer of keratin (at arrow). Histologic picture now points to a low-grade papillary epidermoid carcinoma. (×40.)

Case 2.—N. W., a 17-year-old Negro girl, a primigravida, had a negative Wassermann test. She was seen for the first time when 5 months pregnant. She was admitted to the hospital 3 weeks later with a chief complaint of vaginal bleeding of four days' duration. The cervix presented a papillary, fairly firm, polypoid mass, 2 cm. in diameter, on the exocervix at three o'clock near the external os. Biopsy was taken. She had a normal delivery and at her postpartum check-up 8 weeks later, the cervix was described as posterior, closed, and lacerated.

On July 11, 1947, a biopsy of the cervical lesion was taken.

Microscopic:—Sections reveal a papillary structure composed of hypertrophic, hyperplastic, stratified squamous epithelium, the cells of which are quite regular. It is supported by a delicate connective tissue framework which is infiltrated moderately with small mononuclear cells. Focal areas of spongiosis and transmigration of leukocytes are noted in the epithelium. The epithelium shows a moderate amount of basal-cell hyperplasia.

Diagnosis:—Papilloma of the cervix (Fig. 5).

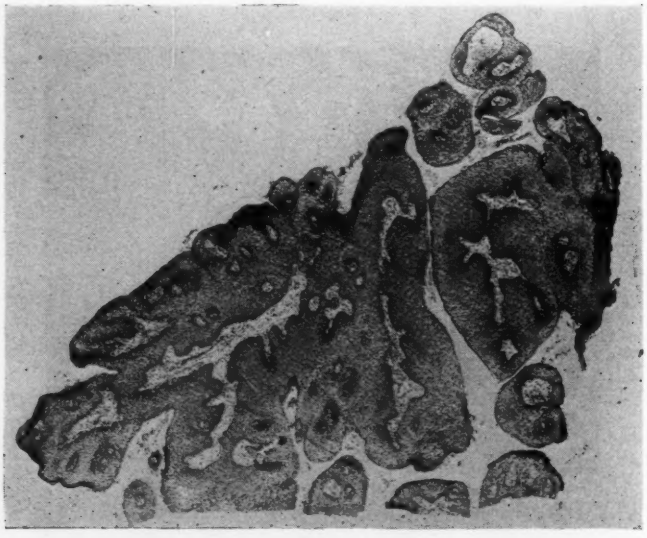

Fig. 5 (Case 2).—Note papillary structures lined by hypertrophic stratified squamous epithelium. (×17.5.)

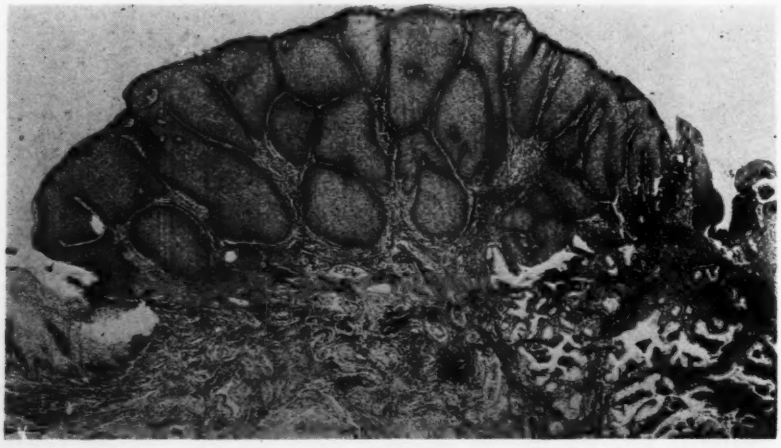

Fig. 6 (Case 4).—Note raised plateau of hypertrophic stratified squamous epithelium. (×17.5.)

CASE 3.—A. P., 22 years old, white, primigravida, with a negative Wassermann test, was seen for the first time when 6 months pregnant. There was a firm, nodular lesion on the anterior lip of the cervix about 1 cm. in diameter and 1 cm. high. Biopsy was taken. The lesion persisted throughout her pregnancy. She had a normal delivery and the lesion was noted at a 3 week post partum checkup. Five months later the growth was described as a large papillary nodule, high on the anterior lip, 1 cm. in diameter. Electric cauterization was carried out. One year later no lesion was visible on the cervix.

On Feb. 5, 1948, a biopsy of the cervical lesion was taken.

Microscopic:—Essentially the same as in the previous case.

Diagnosis:—Papilloma of the cervix.

CASE 4.—F. H., was 20 years old, Negro, gravida 0, para 0, with Wasserman test negative, and vaginal culture negative for the gonococcus. The patient's chief complaint was 3 months' amenorrhea and vaginal bleeding for one week. The uterus was normal in size. The report of a curettage was interval endometrium. At the time of the curettage, the cervix presented a firm, cauliflower-like grayish-white growth, 1 cm. in diameter, at two o'clock on the exocervix near the external os.

On March 18, 1949, a biopsy of the cervical lesion was taken.

Microscopic.—Sections reveal a raised plateau composed of hypertrophic, hyperplastic, stratified squamous epithelium, the cells of which are quite regular. It is supported by a connective tissue framework which is infiltrated moderately with mononuclear cells. The tumor rises in an area between a hypertrophic squamous epithelium on one side and normal columnar epithelium on the other.

Diagnosis.—Papilloma of the cervix (Fig. 6).

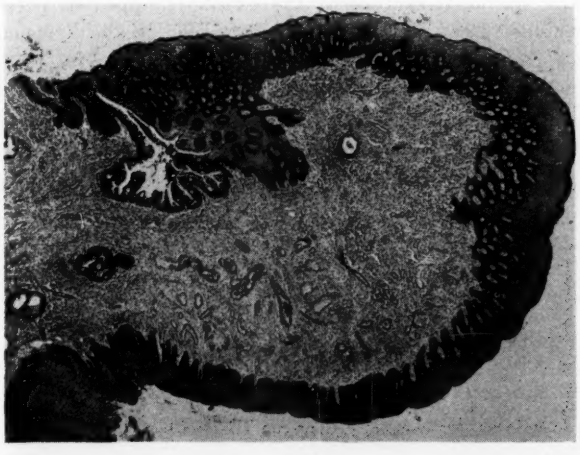

Fig. 7 (Case 6).—Solitary oval papillary structure with hypertrophic stratified squamous epithelium. (×20.)

CASE 5.—I. C. was a 30-year-old Negro woman, nulliparous, with a four plus Wassermann test. The patient's chief complaint was menometrorrhagia of 6 months' duration. Examination revealed a polypoid lesion on the anterior lip of the cervix on May 15, 1945. On Oct. 8, 1945, the patient had a subtotal hysterectomy for large myomas of the uterus. Subsequent checkup in the clinic revealed that the polypoid lesion on the cervix still was present. Biopsy was taken on May 18, 1946. The growth was described as 1.5 cm. in size and consisted of a soft, elevated area with a granular appearance.

On May 18, 1946, a biopsy of the cervical lesion was taken.

Microscopic:—Sections reveal a papillary structure composed of hyperplastic, stratified squamous epithelium, the cells of which are quite regular. It is supported by a connective tissue framework which is extensively infiltrated with inflammatory cells.

Diagnosis:—Papilloma of the cervix with acute and chronic inflammation.

CASE 6.*—D. W., 66 years old, white, para 2-0-0-2, was 22 years post menopause. The Wassermann test was negative. The patient presented herself with a cystocele, rectocele, and a first-degree prolapse. An asymptomatic, 0.5 cm., grayish-white, polypoid sessile growth was noted on the exocervix near the external os. On Aug. 2, 1951, a vaginal plastic procedure was performed, including an amputation of the cervix.

*Grateful acknowledgment is made to Dr. P. Gruenwald, pathologist at Beth-el Hospital, for permission to use this case.

On Aug. 2, 1951, the cervix was amputated in the course of a Manchester vaginal repair.

Microscopic.—Sections reveal a solitary, oval-shaped tumor composed of hypertrophic, hyperplastic, stratified squamous epithelium, the cells of which are quite regular. It is supported by a central core of connective tissue. The prickle-cell layer of the epithelium extends from the basal layer almost to the surface. On the surface there is a two- to three-cell layer of flattened cells. At the base of this tumor are noted several endocervical glands, some with epidermization. One end of the epithelium joins a layer of hypertrophic, stratified squamous epithelium, while the other end runs into endocervical tissue.

Diagnosis.—Papilloma of the cervix (Fig. 7).

CASE 7.—A. C., 23 years old, Negro, para 0-0-1-0, Wassermann negative, was three months pregnant when first seen. Covering the anterior lip of the cervix for an area of about 3 by 1.5 cm. was a raised, irregular, fleshy pink stubblelike lesion, about 0.5 cm. in height. This lesion seemed to consist of one mass of tissue but closer examination soon revealed that it consisted of several separate lesions, each attached to the cervix by a central, fixed stalk. Between the stalks, the epithelial surface of the exocervix appeared perfectly normal. Two small papillary projections, fleshy pink in color, were seen in the hymenal region of the vagina. Both cervical and vaginal lesions were biopsied. On Nov. 7, 1951, an attempt was made to autoinoculate the lesion from the cervix to an uninvolved area on the right perineum.

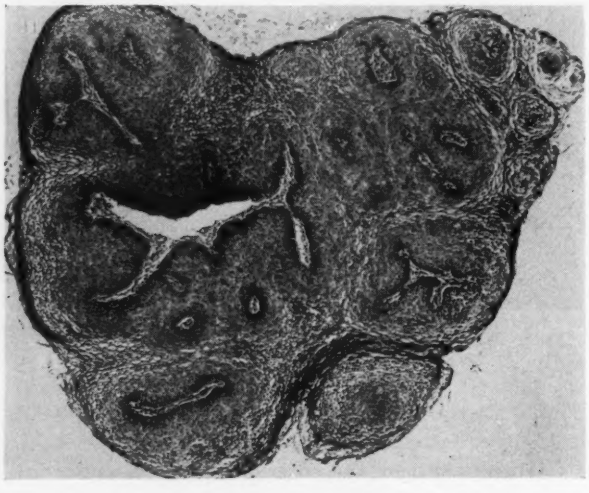

Fig. 8 (Case 7).—One of numerous papillary stalks. (×40.)

In the brief period of observation the autoinoculation did not take. The growths were treated with podophyllin and 3 weeks later the cervix was clean and no lesions were visible grossly on either the cervix or the vagina.

On Aug. 14, 1951, a biopsy of the cervical lesion was taken.

Microscopic.—Sections reveal a papillary structure composed of hypertrophic, hyperplastic, stratified squamous epithelium, the cells of which are quite regular. It is supported by a delicate connective tissue framework which is infiltrated moderately with small mononuclear cells. Focal areas of spongiosis and transmigration of leukocytes are noted in the epithelium.

Diagnosis.—Papilloma of the cervix consistent with condyloma acuminatum (Fig. 8).

CASE 8.—J. T., 22 years old, Negro, primigravida, Wassermann negative, was 18 weeks pregnant when first seen. The vulva presented a large papillary sessile growth on the right labia about 6 by 4 cm. in size, red and firm. A few small similar growths were noted on the

left labia. A similar lesion was noted in the form of a polypoid mass near the os on the anterior lip of the cervix, 3 cm. in diameter. Both cervical and vulval lesions were biopsied. The lesions on the vulva were treated with podophyllin on Aug. 14 and Sept. 11, 1951. They responded favorably with considerable shrinkage and atrophy. On Sept. 20, 1951, an attempt at autoinoculation was made, transferring material from the untreated cervical lesion to the medial aspect of the right thigh. In the brief period of observation the autoinoculation did not take. The cervical growths were treated with podophyllin on Sept. 20, 1951. The patient delivered a living, 3 pound, 8 ounce baby three days later. Three weeks post partum the cervical lesions were gone and the vulval growths had almost disappeared.

On July 26, 1951, a biopsy of the cervical lesions was taken.

Microscopic:—Sections reveal a papillary structure composed of hypertrophic, hyperplastic, stratified squamous epithelium, the cells of which are quite regular. It is supported by a delicate connective tissue framework which is infiltrated moderately with small mononuclear cells. Focal areas of spongiosis and transmigration of leukocytes are noted in the epithelium.

Diagnosis.—Papilloma of the cervix, consistent with condyloma acuminatum (Fig. 9).

Fig. 9 (Case 8).—Numerous papillary structures lined by hypertrophic stratified squamous epithelium. (×15.)

Comment

Ewing's[1] definition of papilloma fails to mention the papillary appearance which so many papillomas present. That this failure is of some importance can be attested by those tumors not composed of pavement epithelium but which have been called papillomas solely because of their papillary appearance, e.g., papilloma of the breast, gall bladder, ovary, stomach, choroid plexus, etc. For purposes of terminology it is suggested that a papilloma be defined as a benign epithelial neoplasm usually composed of pavement epithelium with supporting connective tissue and frequently papillary in structure. Specifically in regard to the cervix, the term papilloma should be limited to benign epithelial neoplasms of stratified squamous epithelium with supporting connective tissue, frequently but not necessarily papillary in structure.

The true nature of condylomata acuminata is obscure. These growths are classified as neoplasms but are considered to have a viral etiology.[13, 14] In addition, they retain the unique property of slowly disintegrating when treated with podophyllin. Since condylomata acuminata are benign papillary neoplasms composed of stratified squamous epithelium, they fall into the classification of papillomas. They are potentially malignant, although rarely. [15, 16] Up to the present time condylomata acuminata of the cervix have been segregated from other papillomas of the cervix merely on the presence or absence of similar lesions elsewhere, usually on the vagina, vulva, or perineum. [17] Te Linde[18] makes the following distinction in discussing lesions of the vulva: "Papillomata are covered with normal appearing epithelium over a tree-like connective tissue core, while condylomata acuminata are covered with markedly hypertrophied stratified squamous epithelium with marked cornification." This may be true of the papillomas and the condylomata acuminata of the vulva but does not carry over in a comparison of the two lesions when found on the cervix. The epithelium of papillomas of the cervix shows hypertrophy and hyperplasia of varying degrees, and the acuminate lesions on the cervix show marked hypertrophy and hyperplasia of the epithelium without any evidence of cornification. If a papillary lesion of the cervix shows hornification, it is more likely a papillary hornifying epidermoid carcinoma of the cervix.[19]

The basic difference between condylomata acuminata and the other papillomas, namely, the transmissibility of the one and the nontransmissibility of the others, offers the most hope for the accurate differentiation of the two lesions on the cervix. However, until such a test is standardized, the best means of differential diagnosis lies in regarding solitary lesions of the cervix with no accompanying genital lesions as papillomas and to consider the others as condylomata acuminata.

Papillomas have been described as having a close association with pregnancy.[8] That this should be so seems unusual. Pregnancy is so frequent and papillomas so rare as to make the relationship a very dubious one. On the other hand 16 of the 31 papillomas were discovered during pregnancy. This may be a reflection of the fact that many women in the childbearing ages rarely are examined vaginally until amenorrhea compels them to seek additional corroborative evidence of pregnancy from a physician. In view of the small number of cases and the difficulties involved in obtaining proper corrective factors, it would be premature to draw any conclusions on the relationship of these tumors to pregnancy.

Considerably more than 31 papillomas of the cervix will have to be studied and followed before any definite conclusions can be drawn as to their behavioristic pattern. Tentatively, however, it would seem that the lesion is benign and responds favorably to excision, cauterization, or podophyllin (the latter if the tumor be of the acuminate variety). Only 3 of the 31 cases can be considered malignant and, of these three, only in the present one (Case 1) is there evidence of distant and continued growth. No evidence has been presented that pregnancy exerts any untoward influence on the behavioristic pattern of these tumors. If the patient is pregnant at the time of discovery, therapy may be instituted promptly or subsequent to the pregnancy, depending on the length of gestation, the local conditions, and the size and location of the lesions.

It is evident that caution must be exercised in the diagnosis and management of papillomas. Since their histological pattern may be atypical, a number of those papillomas whose clinical course was benign originally were judged to be malignant. Complete removal of destruction of the lesions is essential and a period of watchful waiting is necessary before final classification of the lesion is possible. The prognosis should be guarded, but is better when the tumor can be completely removed or destroyed.

TABLE I

AUTHOR	YEAR	CONDYLOMA ACUMINATUM	OTHER PAPILLOMAS	MALIGNANT PAPILLOMAS	TOTAL
Schultz	*	1 (0 preg.)			1
Kleeman	*		1 (0 preg.)		1
Heitzman	*			1 (0 preg.)	1
Meyer	1921	4 (2 preg.)	1 (0 preg.)	1 (0 preg.)	6
Wharton	1921	1 (0 preg.)			1
Mohnle	1923		1 (1 preg.)		1
Cattaneo	1927		1 (0 preg.)		1
Mershon	1938		2 (2 preg.)		2
Treite	1940	2 (2 preg.)	1 (0 preg.)		3
Edmondson et al.	1945		4 (3 preg.)		4
Susan and Meister	1948		1 (1 preg.)		1
Wolfe	1950		1 (1 preg.)		1
Present Series		2 (2 preg.)	5 (2 preg.)	1 (0 preg.)	8
		10 (6 preg.)	18 (10 preg.)	3 (0 preg.)	31 (16 preg.)

*Reviewed in 1921 by R. Meyer.

Summary

The literature on papillomas of the cervix has been reviewed. Eight additional cases have been presented, including one case which showed malignant transformation. The definition of papilloma, its relationship to pregnancy, its malignant potentiality, and the present status of condyloma acuminatum have been discussed.

Grateful acknowledgment is made to Dr. Emil Novak for reviewing the pathologic material presented in this paper.

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441 OCEAN AVENUE.

OBSERVATIONS UPON THE ROLE OF THE SEX HORMONES IN THE DEVELOPMENT OF BONY PELVIC CONFORMATION

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IN A study published in 1942 by Morton and Hayden, it was shown roentgenographically that, except for minor differences, the bony pelves of male and female children were of similar and undeterminate type before the age of puberty. In adolescence contemporaneously with the maturation of the secondary sexual characteristics, the bony pelves also developed characteristically and differently in the two sexes. This led us to wonder if the sex hormones, which first appear in significant amount shortly before puberty, might play a major role in producing the sexual characteristics of adult pelves, even though it was appreciated that the fundamental determinant might well be chromosomal. Several observers[1, 2, 3, 4] in the past have studied fetal pelves directly and concluded that sexual differences existed even at this early stage. If true, the sex hormones would seem to be excluded as determinants of pelvic shape. While Morton and Hayden also found minor differences in the pelves of children of different sexes, we submit that the pelves of prepuberal children are remarkably alike and that there is a striking dissimilarity in the two sexes after puberty. What role do the sex hormones play in producing these changes?

In order to gather evidence bearing on this question, a roentgenographic study of the pelves of individuals exhibiting marked sexual immaturity was attempted. If the sex hormones actually play a major role in producing the characteristics of the adult pelves of the two sexes, such individuals should have pelves of the undeterminate, preadolescent type, or, at least, pelves which differ from the normal. Thus far it has been difficult to obtain relatively young individuals in this category who have not already undergone rather extensive treatment.

Material

It has been possible to study roentgenologically the pelves of 13 hypogonadal males between the ages of 17 and 43 years and 5 hypogonadal females between the ages of 15 and 30 years. All of the males gave a history of failure to develop sexually at the normal age of puberty, or thereafter, without the aid of male sex hormone administration. In all instances there was evidence of hypogonadism with failure of development of normal secondary sexual characteristics. The hypogonadism was of hypophyseal origin in 9 cases, in two of which pituitary tumors were responsible. These patients were typical examples of hypophyseal infantilism, hypophyseal eunuchoidism, primary

testicular eunuchoidism, and Klinefelter's syndrome. Of the female patients, 3 were examples of ovarian agenesis, one had been castrated at 7 years of age, and one was suffering from hypophyseal infantilism. Clinical descriptions are noted in Table I together with determinations and assays of urinary gonadotrophin (FSH).

Before describing the characteristics of these pelves, a brief review of the chief differences between the adult pelves of the two sexes is given in order that the reader may interpret the findings more readily. The bones of adult male pelves are much heavier and more massive than those of the female. The male pelvis is higher, and its side walls usually converge slightly toward the outlet; the subpubic arch is narrow, and usually the lower portion of the sacrum bends forward to narrow further the pelvic outlet. The sacrosciatic notch is usually narrower than that of the female, though this is variable. The shape of the male pelvic inlet is that of a "blunt heart," rather than a smooth ovoid as in the female; the greatest transverse diameter of the inlet is closer

A. *B.*

Fig. 1.—*A*, Pelvic inlet of a girl, aged 7 years. *B*, Pelvic inlet of a boy, aged 7 years. Both show elongation of the anteroposterior diameter of the inlet and inward bowing in the acetabular regions. Though of opposite sexes, the two pelves are quite similar.

to the sacral promontory, diminishing the size of the posterior segment of the pelvis. The anterior portion of the inlet is elongated anteroposteriorly and narrows toward the symphysis. When we speak of an android inlet, anterior or posterior, we are referring to these features, as they pertain to the anterior or posterior segments of the inlet.

The principal characteristics of the "undeterminate" preadolescent pelvis as determined in a previous study of children's pelves are an elongated inlet, with the anteroposterior diameter exceeding the greatest transverse diameter, inward bowing of the acetabular regions (at the inlet), light bones, medium subpubic arch, rather high pelvis (Fig. 1).

The results of the study are given in tabular form; in Table II are listed the male patients who had received androgenic therapy prior to study, in Table III are listed those who had received no therapy at the time of the roentgenographic examination. It should be noted that the androgenic therapy was quite effective in the respect that it produced increased growth of pubic and

TABLE I. DETAILS OF RESULTS

SUBJECT	AGE IN YEARS AT START OF THERAPY	AGE IN YEARS AT TIME OF X-RAY FILMS	DIAGNOSIS	17 KETOSTEROIDS IN MG./24 HR.	OTHER EVIDENCE OF DEFICIENT SEXUAL DEVELOPMENT	PELVIC INLET	SACROSCIATIC NOTCH	PELVIC OUTLET	TYPE OF PELVIS
A. (Androgenic therapy for 1 year)	25	26	Familial hypogonadotrophic eunuchoidism	10.6	Infantile penis, high voice, no facial or pubic hair. Impalpable prostate. Small soft testicles, right cryptorchism. Tall, long extremities. Bone age 16-18 years. FSH neg. at 5 M.U.	Android (with slight bowing-in of acetabular regions)	Medium	Narrow, converging side walls. Heavy bones	Android
B. (Androgenic therapy for 2½ years. Inert preparations for 1½ years)	17	20	Same as above		Essentially the same clinical evidences as above. Right cryptorchism. Bone age 12-15 years. FSH neg. at 5 M.U.	Android	Medium	Narrow, converging side walls. Heavy bones	Typically android
C. (Androgenic therapy for 8 months)	29	29	Same as above	5.5	Essentially the same. Migratory testes. Bone age 19-20 years. FSH neg. at 5 M.U.	Gynecoid (possibly greatest transverse diameter is closer to sacrum)	Wide	Narrow. Heavy bones	Mixed
D.	22	22	Hypophyseal infantilism	1.8	Small stature. Infantile external genitals, rudimentary prostate. No hair on chest, face, or pubis. Bone age 15-16 years. High voice. FSH neg. at 5 M.U.	Android-anthropoid. Inward bowing in acetabular regions	Wide	Medium, 60 degrees. Converging side walls, high	Mixed
E.	22	22	Panhypopituitarism	1.4	FSH neg. at 5 M.U. Bone age 14-15 years	Android-anthropoid	Medium	Narrow, 55 degrees. Heavy bones. High	Android-anthropoid AP—12 Th.—11.8
F. (Androgenic therapy for 3 years)	19	22	Preadolescent testicular eunuchoidism	8.6 FSH pos. at 6 neg. at 18	High voice. Sparse beard. Small penis. Tall. Long extremities. Prostate "extremely small." Bone age 17-18 years	Android	Narrow	Narrow. Heavy bones	Android
G.	32	36	Preadolescent	8.5	High voice. Sparse	Android-	Narrow	Narrow. Heavy	Android-

G. (Androgenic therapy for 4½ years)	32	36	Preadolescent testicular eunuchoidism	8.5	High voice. Sparse beard. Small penis. Tall. Long extremities. Right testis in canal, left not palpable. Prostate small. FSH pos. at 96 M.U. Bone age 16-18 years	Android-gynecoid	Narrow	Narrow. Heavy bones	Android-gynecoid
H. (Androgenic therapy for 3½ years)	32	35	Preadolescent testicular eunuchoidism	13.3	Sparse beard. Small penis. Tall. Long extremities. Right cryptorchism. Left testis rudimentary. Bone age 25 years. Prostate small. FSH pos. at 5 M.U., neg. at 80 M.U.	Android-gynecoid		Narrow. Bones light like female	Android-gynecoid
I. (Androgenic therapy for 1 year)	34	35	Hypogonadotrophic eunuchoidism (pituitary tumor)	3.8	Infantile external genitals. No pubic or facial hair. Long extremities. Bone age 14-15 years. FSH neg. at 3 M.U.	Android		Narrow. Heavy bones	Android
J.	17	17	Hypogonadotrophic eunuchoidism (pituitary tumor)	0.5	Infantile external genitals. No pubic or facial hair. Long extremities. Bone age 12-15 years. FSH neg. at 5 M.U.	Android (with slight inward bowing in acetabular regions)	Wide	Narrow. Heavy bones. High	Android (rather wide anterior half)
K.	21	21	Klinefelter's syndrome with hypogonadism		Tall. Small penis and testes; gynecomastia; no facial, sparse axillary and pubic hair. Testicular biopsy showed tubular atrophy with Leydig cell hyperplasia. Bone age 17-18 years. FSH pos. at 80 units	Android	Narrow	Narrow. Heavy bones	Android
L.	37	37	Hypophyseal infantilism		FSH neg. Short; no sexual characteristics	Android-anthropoid (inward bowing)	Medium	Narrow. Tall. Fairly heavy bones	Android-anthropoid

TABLE I—CONT'D

SUBJECT	AGE IN YEARS AT START OF THERAPY	AGE IN YEARS AT TIME OF X-RAY FILMS	DIAGNOSIS	17 KETOSTEROIDS IN MG./24 HR.	OTHER EVIDENCES OF DEFICIENT SEXUAL DEVELOPMENT	PELVIC INLET	SACROSCIATIC NOTCH	PELVIC OUTLET	TYPE OF PELVIS
M.	31	43	Hypogonadotrophic eunuchoidism	1.4	Tall. Long extremities. Infantile penis and testes. Sparse axillary and pubic hair. Bone age 18 years (chronological 31). FSH neg. at 5 M.U.	Android-gynecoid. Rounded anterior segment		High. Narrow, 55 degrees. Heavy bones	Android-gynecoid
(Androgenic therapy for 3 years)									
N.	30	30	Ovarian	21.5	No vagina (has artificial one), no uterus, tubes, ovaries (at peritoneoscopy). Small breasts, sparse pubic and axillary hair. Feminine form. Weight 128 pounds, height 5 feet, 7½ inches	Gynecoid	Wide	Wide, 110 degrees. Light bones	Gynecoid
O.	15		?Ovarian agenesis		Short, obese, underdeveloped secondary sexual characteristics. Never menstruated. Bone age 14-15 years	Android (greatest transverse diameter is near sacrum)	Medium	Narrow, 60 degrees. Light bones, converging side walls	
P.	33	33	Castrated at age of 7		FSH high. No sexual characteristics. Bone age ? 21 years	?Android, posterior half. Gynecoid, anterior half	Medium	Narrow	?Android-gynecoid
	39	(After treatment with estrogens)					(about same, but larger)		
Q.	18	18	Hypophyseal infantilism		Short. No sexual characteristics. No FSH. Bone age 12½ years	?Android posterior inlet; gynecoid ant. inlet	Narrow	Narrow	?Android-gynecoid
R.	17	16	Ovarian agenesis		Short, 4 feet. Lack of secondary sex characteristics	Gynecoid inlet (inward bowing in acetabular regions)		Wide. Light bones	Gynecoid

axillary hair, growth of the penis, relatively normal libido, nocturnal emissions, and an increased sense of well-being in all of the patients to whom it was administered.

TABLE II. FINDINGS IN CASES IN WHICH THE PATIENTS HAD BEEN TREATED WITH ANDROGENS

MALE SUBJECTS	AGE IN YEARS AT FIRST EXAM.	DURATION OF TREATMENT	BONE AGE	PELVIC CHARACTERISTICS		
				ANDROID FEATURES	PREPUBERTY FEATURES	GYNECOID FEATURES
A.	26	1 year	16-18 years	Inlet Heavy bones Narrow arch	Inward bowing at inlet	–
B.	20	2½ years	12-15 years	Inlet Heavy bones Narrow arch	–	–
C.	29	1 year	19-20 years	Posterior inlet Heavy bones Narrow arch	–	Anterior inlet
D.	22	3 years	17-18 years	Inlet Heavy bones Narrow arch	–	–
E.	36	4½ years	16-18 years	Posterior inlet Heavy bones Narrow arch	–	Anterior inlet
F.	35	3½ years	25 years	Posterior inlet Narrow arch	–	Anterior inlet Light bones
G.	43	12 years	18 years	Posterior inlet Heavy bones Narrow arch	–	Anterior inlet
H.	35	1 year	14-15 years	Inlet Heavy bones Narrow arch	–	–

TABLE III. RESULTS IN CASES IN WHICH THE PATIENTS HAD RECEIVED NO ANDROGENIC THERAPY AT THE TIME OF THE EXAMINATION

MALE SUBJECTS	AGE IN YEARS AT FIRST EXAM.	BONE AGE	PELVIC CHARACTERISTICS		
			ANDROID FEATURES	PREPUBERTY FEATURES	GYNECOID FEATURES
D.	22	15-16 years	Posterior inlet High pelvis Converging side walls	Inward bowing	Anthropoid anterior pelvis. Light bones
E.	22	14-15 years	Posterior inlet Heavy bones Narrow arch	–	Anthropoid pelvis
J.	17	12-14 years	Posterior inlet Heavy bones Narrow arch	Inward bowing	Rather wide anterior pelvis
K.	21	17-18 years	Inlet Heavy bones Narrow arch	–	–
L.	37	?	Posterior inlet Heavy bones Narrow arch	Inward bowing	Anthropoid anterior inlet

In all 13 male patients, both treated and untreated, the pelves showed unmistakable signs of android features. The diagnoses were:

Android pelvis	6
Android-gynecoid	4
Android-anthropoid	3

While accurate measurements were not possible, the greatest transverse diameter of the inlet appeared to be closer to the sacrum than in the female in all instances. As seen in the foregoing, the anterior segment of the pelvic inlet was somewhat more rounded in 7 of the 13 cases than is usually observed in the typically android pelvis. In 2 of the 13 patients the bones were light like those of the female. In all cases the pelves were high and the subpubic angle was narrow. In 5 instances the preadolescent characteristic of inward bowing in the acetabular regions was present (Fig. 2). The sacrosciatic notch was variable and not characteristic.

It is not possible to determine whether the androgenic therapy influenced the bony pelves, effective though it was in other respects. The pelves of the 13 patients showed distinct androgenic characteristics. However, in the group of 8 treated patients, only one showed evidences of the preadolescent state (inward bowing), and 4 showed possible evidences of gynecoid features in the forepelvis, while in the group of 5 untreated patients, 3 showed the preadolescent characteristic and 4 exhibited some gynecoid features in the forepelvis. While these results rather suggest that androgenic therapy actually affected the development of the bony pelvis in this group of individuals, it seems inconceivable that this could be the case, since the youngest age at which it was started was 20 years, when ordinarily the pelvis has already acquired its adult form. However, it should be pointed out that in all instances the bone age was considerably less than the chronological age though not under the 12 to 15 year level in any case.

TABLE IV. RESULTS IN FIVE FEMALES

FEMALE SUBJECTS	AGE (YEARS)	BONE AGE	DIAGNOSIS	PELVIC CHARACTERISTICS		
				ANDROID FEATURES	PREPUBERTY FEATURES	GYNECOID FEATURES
N.	30		Ovarian agenesis	–	–	Inlet Light bones Wide arch
O.	15	14-15 years	Ovarian agenesis	Inlet Narrow arch	–	Light bones
P.	33	21 years	Castrated at age of 7	? Posterior inlet Narrow arch	–	Anterior inlet Light bones
Q.	18	12½ years	Hypophyseal infantilism	? Posterior inlet Narrow arch	–	Anterior inlet
R.	17		Ovarian agenesis	–	Inward bowing	Inlet Light bones Subpubic arch

Results in Females.—

The results in the 5 females are given in Table IV. The pelves were difficult to classify accurately, though the first patient (aged 30 years) with ovarian agenesis had a typical gynecoid pelvis (Fig. 4). In addition, she ex-

Fig. 2.—Pelvis of last subject in Table III. He was 37 years old and showed well-marked evidences of hypophyseal infantilism. He had received no treatment. This pelvis was regarded as having the following android features: (1) shape of posterior segment of inlet, (2) heavy bones, (3) narrow pubic arch. It also shows the prepuberal features of inward bowing in the acetabular regions and a rather more rounded anterior segment of the inlet than is usual in the male.

Fig. 3.—Typical android pubic arch in a 43-year-old patient with hypogonadotrophic eunuchoidism who had received androgens for one year.

Fig. 4.—Female, aged 30 years, with ovarian agenesis. This is the pelvis of Subject N in Table IV. Typical gynecoid features.

hibited many other "female" characteristics. She was 5 feet, 9½ inches tall and weighed 128 pounds. Her general appearance and proportions were typically feminine, though the breasts were small and pubic and axillary hair was scanty. An artificial vagina had been created because of total absence of the vagina. The patient was married and experienced satisfactory coitus. Peritoneoscopy showed that uterus, tubes, and ovaries were absent.

In all five instances the bones were light and suggested the female; there were android features in addition in 3 of them.

Comment

The evidence presented is incomplete, and it is obvious that serial studies upon younger individuals of each sex, both with and without treatment, would have to be made in order to draw definite conclusions. However, the results strongly suggest that the characteristics of the adult bony pelves of both sexes are not dependent primarily upon normal concentrations of the sex hormones. Nevertheless, it is entirely possible that the sex hormones exert some effect in bringing the pelvis to its mature form. Perhaps we are born with pelves which are male or female, as our genitals are male or female, but without an adequate concentration of the appropriate gonadal hormone these structures do not reach their full development. In any event, before puberty, male and female pelves are remarkably alike, while after puberty they are definitely dissimilar.

It is of great interest that in this group of individuals all of whom showed either the absence of, or marked deficiencies in, the second sexual characteristics, the pelves retain unmistakable attributes of the appropriate sex. Perhaps roentgen examination of the pelvis would be of material assistance in determining the true sex of pseudohermaphrodites. Imagine what it would show in the case of a true hermaphrodite!

Summary

The bony pelves of 13 males and 5 females who exhibited the absence of secondary sexual characteristics because of disease or deficiency of the anterior pituitary gland, or because of absence or functional deficiency of the gonads, were studied roentgenologically. In all instances some of the characteristics appropriate for the particular sex were observed, though in not a few stigmas of incomplete development and characteristics of the opposite sex were present also. It was concluded that the sex hormones are not the primary determinants of the sexual characteristics of the bony pelvis, though it was conjectured that they may aid in the maturation of the pelvis in the proper direction, and, indeed, the possibility of the variations in the shape of adult pelves sometimes being on a hormonal basis cannot be dismissed.

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SCARS OF THE PREGNANT AND NONPREGNANT UTERUS*†

I. Histologic Comparison of Scars Two Weeks Postoperatively

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INCISIONAL scars of the uterus are the result principally of two operations: myomectomy and cesarean section. Scars of the cervix and scars resulting from myomectomy during pregnancy will not be discussed in this paper.

Postmyomectomy and Postcesarean Scars: Incidence of Rupture in Subsequent Pregnancies

During pregnancy or labor, the uterus may burst open in the vicinity of the uterine scar. The baby or the mother or both may succumb. Whether the uterus ruptures or not during pregnancy or labor may be considered a test of the integrity of the uterus. The incidence of rupture of the uterus following cesarean section varies with different authors.[1-7] There are approximately 4 per cent ruptures of the classical cesarean section scar and about 0.25 per cent after low cervical cesarean section. As pointed out by Dieckmann[8] and by Bill,[9] these figures cannot be accurate because: (1) the total number of cesarean sections is not always stated by the author; (2) the subsequent obstetric history of the patients is not stated; (3) silent ruptures found at time of operation are often not reported; (4) recoveries after rupture of the uterus are reported more frequently than mortalities; (5) the higher incidence of repeat cesarean sections reduces the incidence of ruptures.

The merits of low cervical section versus classical section will not be discussed here except that it may be stated that the low cervical operation is advocated preponderantly in the literature. The majority of obstetricians advise routine repeat cesarean sections.[10] However, Schmitz and Gajewski,[11] as exponents of the minority group, allow delivery from below in selected cases under proper supervision.

The incidence of rupture of a postmyomectomy scar during pregnancy or labor is difficult to ascertain. Ahltorp[12] reports an incidence of 1.5 per cent in the literature. This figure may or may not be correct since cases in which recovery occurred are frequently reported, the fate of all patients who have had myomectomies is not known, and the extent of the operation is variable with resultant variability of the scar.

Incidence of Repeat Cesarean Section Following Myomectomy and Cesarean Section

A comparison of the incidence of repeat cesarean section and cesarean section following myomectomy shows that while some writers consider a postmyomectomy scar as dangerous as a postcesarean scar,[13] the majority of operators consider the myomectomy scar more capable of withstanding pregnancy and labor than a cesarean section scar. Thus, Counseller[14] reports only 4

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cesarean sections performed on 68 patients who had myomectomy done before pregnancy, Finn[15] reports only 17 per cent cesarean sections on women with previous myomectomies, and Mussey[16] reports 9 per cent. In contrast, the incidence of repeat cesarean section in the most conservative hands is 67 per cent.[11]

Effect of Uterine Scars on Fertility

Dieckmann[8] believes that a cesarean section lowers the patient's subsequent fertility only slightly, whereas Bride[17] states that 14 per cent of his patients who had had cesarean section subsequently had abortions, and the incidence of sterility was 35 per cent. Finn[15] reports a 20 per cent abortion rate following myomectomy performed before pregnancy, and sterility in 75 per cent. A comparison of such statistics is obviously conjectural since many of the myomatous uteri would not have become pregnant without myomectomy.

Normal Healing

The mechanism of normal healing in general may be briefly discussed before mentioning the factors responsible for the so-called weak scar. The sine qua non of wound healing is formation of connective tissue. Hartwell[18] summarizes our knowledge of wound healing as follows: (1) There is no healing outgrowth of fibroblasts or fibers from pre-existing structures. (2) A healing cicatrix is formed by the exudate cells or the macrophages called by different names, as clasmatocytes, polyblasts, histiocytes, and epithelial leukocytes. (3) Fat, instead of being a tissue inert in or inimical to the healing process, is of great importance in the furtherance of healing. (4) Determination of the healing fibrosis is directly related to physical forces. (5) The blood lymphocyte is apparently the true healing cell, acting as both macrophage and fibroblast.

Healing in the Pregnant Uterus

The concept held by Williams[19] that an incision into the uterus heals by regeneration of the muscle fibers has gradually given way to the knowledge that healing occurs by fibrous tissue formation. It is true that Hofbauer[20] has demonstrated mitosis of the nuclei of muscle fibers, but this occurs only in the outer layers of the myometrium and plays an insignificant role in healing. Schwarz, Paddock, and Bostnick[21] have clearly demonstrated that healing in the pregnant uterus occurs by connective tissue formation. They describe the process as follows: After an incision, there is an exudate between the edges, then fibrin formation, then fibroblastic proliferation and scar tissue deposit. This scar tissue shrinks, pulling the muscle edges together until the scar becomes almost imperceptible. They claimed that new fibroblasts develop by proliferation of the interstitial tissue.

Healing in the Nonpregnant Uterus

While healing of incisions in the pregnant uterus has been studied thoroughly by many competent observers,[22-28] scars in nonpregnant uteri are not easily available for study since it is difficult to obtain a surgical specimen of a nonpregnant uterus which has had a previous hysterotomy in the nonpregnant state. A search of the literature reveals only one article, by Monroe Kerr,[28] in which a comparison is made of wounds in pregnant and nonpregnant uteri. However, the only nonpregnant uterus mentioned was one perforated by a uterine dilator. Sections of the healed area revealed a mass of connective tissue with scattered areas of muscle bundles. Kerr believed that if the gap in the uterus is small, it may be bridged over by muscle elements. Because of the lack of previous study of healing in the nonpregnant uterus, this paper will

attempt to answer the question: Does an incision into a pregnant uterus heal differently than one made into a nonpregnant uterus?

Procedure

Under Nembutal anesthesia, laparotomies were performed on female dogs. The bicornate uterus was delivered and several longitudinal incisions were made into each horn. Each incision was approximately 2.5 cm. in length and extended into the lumen of the uterus. The incision was then closed with a continuous 4-0 chromic suture. After the uterus was replaced, the abdominal incision was closed and the dog maintained for a period of exactly two weeks. A total hysterectomy was then performed and cross sections were made from each area of incision. The sections were stained by the orcein-van Gieson technique.

Fig. 1.—Nonunion, nonpregnant uterus 2 weeks postoperatively, cross section of longitudinal incision. (×16.) Failure of healing due to infection.

A similar procedure was used on pregnant dogs. When the dog seemed to be at term by palpation, a laparotomy was performed under Nembutal anesthesia. Each fetal swelling was incised longitudinally for a distance of approximately 4 cm. The fetus, membranes, and placenta were removed and the uterine incision closed as in the nonpregnant dog. The animal was maintained for two weeks, after which a hysterectomy was performed and histologic studies were made of the uterine incisions. The orcein-van Gieson stain was used because it colors connective tissues red and muscle fibers yellow. This color differentiation shows up nicely in the colored slides. In the black and white photomicrographs, the connective tissue is almost black in color.

Comparison

The pitfalls of histologic study of uterine scars are numerous. Isolated sections are not always representative of the entire scar. Artifacts are numerous and confusing. Histologic integrity does not always reflect functional capacity. Microscopic study must always consider union of multiple directional muscle layers of the uterus.

In this study four pregnant and four nonpregnant dogs were used. A minimum of four incisions was made in the uterus of each animal so that comparisons were made between 16 sites of wound healing in the pregnant and nonpregnant uteri. The photomicrographs present the salient features of this comparison and represent typical conditions of each group.

Fig. 2.

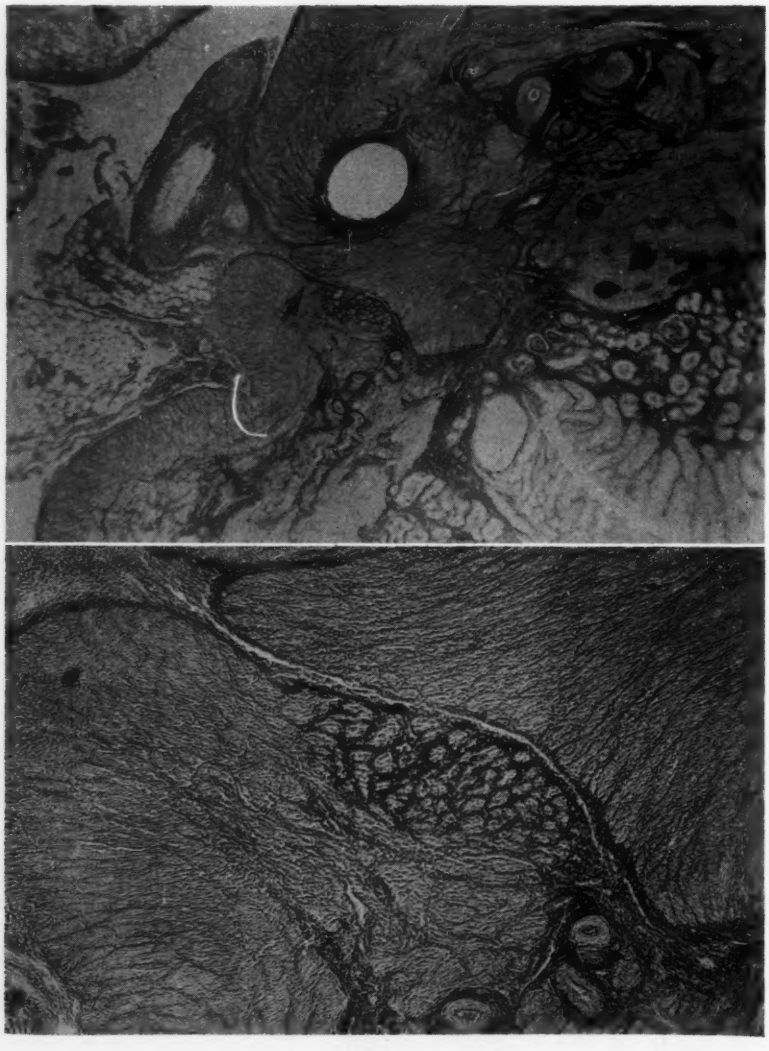

Fig. 3.

Fig. 2.—Nonpregnant uterus. Cross section of longitudinal incision, 2 weeks postoperatively. Arrow points to healing line. (Orcein-van Gieson stain, ×16.) See Fig. 3.

Fig. 3.—Nonpregnant uterus. Higher power (×100) of area of arrow seen in Fig. 2. Note slight amount of connective tissue present in the healing line. Orcein-van Gieson stain. The connective tissue is almost black in these photomicrographs. In the colored slides the connective tissue stains red in color, the muscle yellow.

The scars of the nonpregnant uteri resemble those of pregnant uteri except in degree. The nonpregnant uterine scars (Figs. 1, 2, 3, 6, 7) have much less connective tissue formation, are thinner, and much less cellular. The scars of the pregnant uteri (Figs. 4, 5, 7) are characterized by richly cellular stroma

and large amounts of connective tissue. The interstitial connective tissues run into the connective tissue of the scar like tributaries feeding a river.

Comment

It seems almost incredible that after a cesarean section the uterus will involute to a 2 ounce mass of tissue, maintaining proximity of the edges for many years, only to burst open during the next pregnancy or labor. Kerr[28] empha-

Fig. 4.

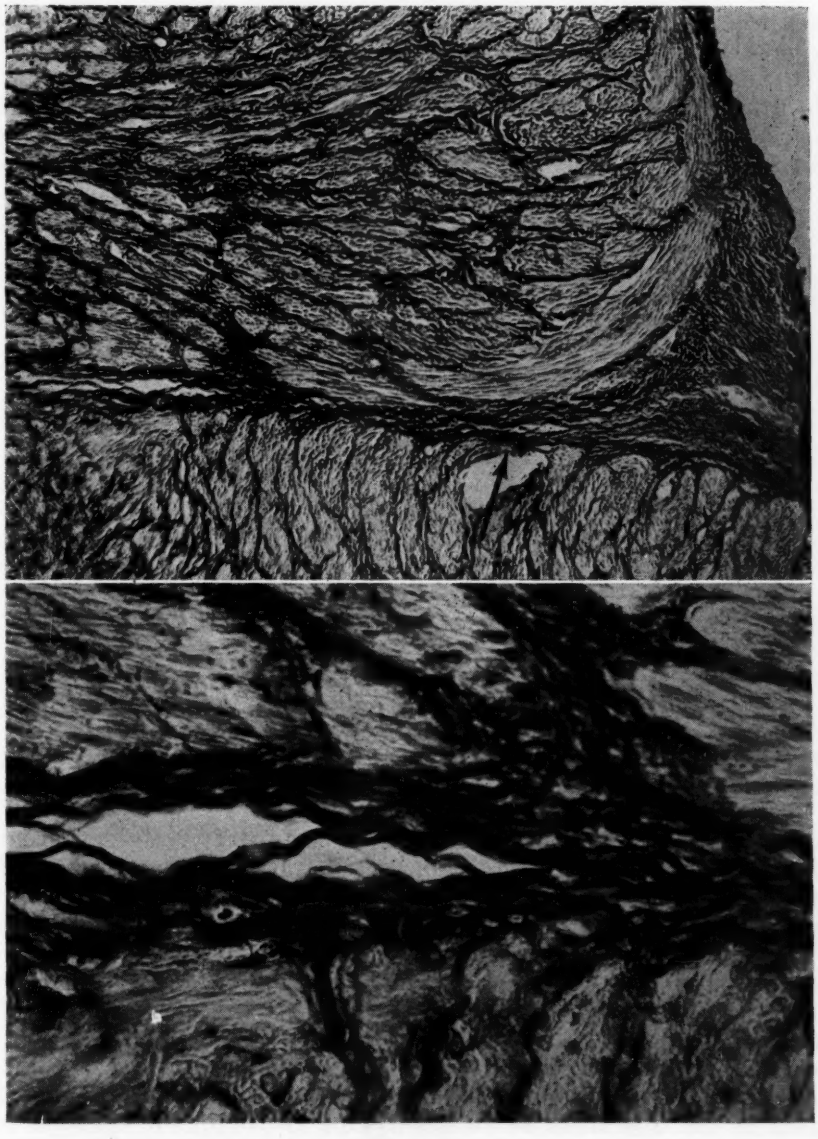

Fig. 5.

Fig. 4.—Pregnant uterus, cross section of longitudinal incision, 2 weeks postoperatively. Arrow points to line of union. Orcein-van Gieson stain. Connective tissue which appears black is abundant. Note abundant interstitial connective tissues which appear as tributaries feeding the main line of healing. (×100.)

Fig. 5.—High-power of Fig. 4 in vicinity of arrow. Note richly cellular connective tissue of healing incision with tributaries of the interstitial connective tissue. (×430.)

sizes and many American writers have re-emphasized the reasons for the hazard in the cesarean section scar. Healing is said to be disturbed by infection, activity of the uterus post partum, improper suturing, the necessity of using coaptive and hemostatic sutures simultaneously, interposition of the endometrium, constitutional diseases, the marked catabolic process of involution which is, theoretically, at least, opposed to the formation of new scar tissue—all these have been considered as influencing adversely the healing of a cesarean incision. The reasons why postmyomectomy scars are much less likely to rupture than cesarean scars have been emphasized by Greenhill[29]: The nonpregnant uterus is at rest. Infection is less likely to occur and less tight suturing is necessary to control bleeding. It might be added that few statistics are available as to the relationship of the depth of incision in myomectomy to the integrity of the uterine scar in a subsequent pregnancy. Most writers state that there is little danger of rupture of a postmyomectomy scar.[30] Munnell and Martin,[31] in a series of 44 cases of postmyomectomy deliveries, performed 4 cesarean sections. In 3 of these myomectomy incisions were close to or into

Fig. 6.—Nonpregnant uterus, cross section of longitudinal incision, 2 weeks postoperatively. Arrow points to thin scar. This would be considered as a case of good union. (Orcein-van Gieson stain. ×16.)

the uterine cavity. The authors state that postoperative infection is more of an indication for subsequent cesarean section than the extent of the myomectomy incision. Ahltorp,[12] in a series of 282 myomectomies, reported entering the uterine cavity in five. All 5 patients delivered subsequently from below. Ahltorp does not consider myomectomy any hazard to subsequent deliveries.

Finn and Muller[15] report 432 myomectomies, among which in 30 the uterine cavity was opened. Twenty-three patients were followed up: 5 had full-term pregnancies; of these, 3 delivered by cesarean section and 2 from below. Two other cesareans were done on patients whose uterine cavities were not opened. The indications were previous myomectomies. These authors consider the magnitude of the operation as an influencing factor in the decision for doing a cesarean section.

It is apparent that the depth and length of the incision are definite factors which must be considered. Thus, it is obvious that the removal of a pedunculated subserous fibroid does not disturb the integrity of the uterine wall. Scars resulting from incisions into the wall of the uterus will test the integrity of the

uterus in a more severe fashion directly proportional to the length, depth, and number of incisions. It must be emphasized also that the incidence of postoperative infections increases as the endometrium is approached by the incision. When the cavity of the uterus is opened during a myomectomy, we have a striking similarity to that of a cesarean section. Greenhill[29] emphasized that postmyomectomy rupture of the uterus occurs rarely because the incision employed seldom enters the cavity of the uterus and he does not include postmyomectomy scar in his list of indications for cesarean section.

Fig. 7.

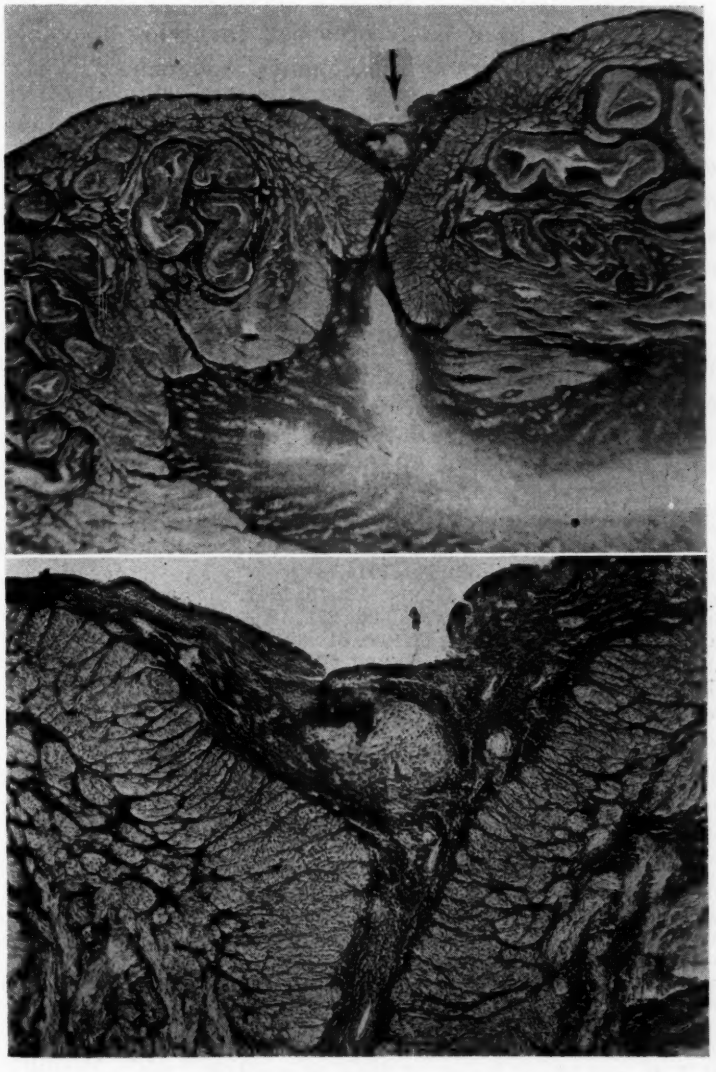

Fig. 8.

Fig. 7.—Pregnant uterus, 2 weeks postoperatively, cross section of longitudinal incision. Arrow points to area of healing. Note abundant connective tissue formation despite turning in of edges of wound. (Orcein-van Gieson stain. ×16.) See Fig. 8.

Fig. 8.—Increased magnification of Fig. 7 showing abundant connective tissue composing scar. Note how the interstitial connective tissue of the muscle bundles join the scar like tribuaries of a river. This apparent active proliferation of the interstitial tissue is considered the prime factor in wound healing in the uterus. This is more apparent in the pregnant uterus because of the marked increase in the interstitial connective tissue. (Orcein-van Gieson stain. ×100.)

Summary

The experimental work presented involves only a single factor of the problem of uterine scars. Evidence has been presented that abundant connective tissue is produced after incision into the pregnant uterus. Healing in the nonpregnant uterus is similar to that in the pregnant uterus except that the scar of the former is thinner. The explanation for the large amount of connective tissue in the wounds of pregnant uteri may be: (1) the marked vascularity resulting in formation of large numbers of fibroblasts, or (2) proliferation of the interstitial connective tissue which is increased during pregnancy. Further work along these lines is in prospect, involving longer postoperative periods and the testing of scars by subsequent pregnancies.

Conclusions

On the basis of the data presented, as a preliminary report of the comparison of wound healing in the pregnant and nonpregnant uterus of the dog, the following conclusions may be drawn:

1. Connective tissue formation following incision into the pregnant uterus is abundant and larger in amount than in the nonpregnant uterus.

2. On the basis of the amount of connective tissue formed, given comparable incisions, the postmyomectomy scar should be given consideration equal to that of the postcesarean section scar in so far as subsequent pregnancy is concerned.

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THE HEPATORENAL SYNDROME COMPLICATING PREGNANCY*

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THE simultaneous occurrence of severe liver and kidney disease during pregnancy to produce the clinical picture described in the literature as the hepatorenal syndrome is relatively rare.[1] According to most authorities, the syndrome exists on purely clinical grounds and has no specific pathological counterpart.[25, 26] However, Lichtman[25] and other recent writers[26, 28, 30] are agreed that the lesions most often found at autopsy of patients who die with this clinical picture are those of lower nephron nephrosis and acute or subacute liver necrosis due to a nonspecific hepatitis.

Although most emphasis in the literature has been placed on the anuria and renal pathology that help to make up this syndrome, it is to be remembered that serious liver damage can also occur. Bywaters,[30] one of the original describers of the crush syndrome, has recently reported central or mid-zonal liver-cell necrosis in 42 patients who died of uremia following crush or other skeletal injury. A recent review of the literature compiled on acute yellow atrophy of the liver associated with pregnancy has added confirmation to the evidence already accumulated incriminating infectious hepatitis as the initial disease process in such cases.[1] A similar pathological picture has been described as occurring in males and in the nonpregnant state.[1] Recovery of the patient with acute yellow atrophy of the liver during pregnancy has been reported but is exceedingly rare.[2]

Much interest has also been focused on the effect of hemorrhage and the resultant anoxia of the liver parenchyma as a cause of hepatic failure following obstetric accidents.[3, 7-11] Govan and MacGillivray,[3] from a thorough study of liver lesions found in 63 cases of fatal obstetric shock, concluded that the extent of initial liver necrosis due to anoxia was directly proportional to the severity of the trauma producing the fatal accident. They strongly recommended that immediate repeated transfusions of whole blood be given in order to prevent irreversible shock and a fatal outcome in such cases. The use of pituitary extract during the latter stages of shock was also considered to be contraindicated.

Javert and Morrison[5] have emphasized the importance of determining the exact etiology of jaundice during pregnancy. They stress the energetic and prompt treatment of all medical and surgical conditions producing clinical and latent jaundice with special emphasis on the conservative management of hyperemesis as a means of preventing the occurrence of acute yellow atrophy of the liver associated with pregnancy. Nixon and associates[6] from a study of 12 icteric and 9 nonicteric pregnant women by means of liver biopsy, discovered two distinct types of jaundice, one related to pregnancy without strik-

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ing changes in the liver, and the other concomitant jaundice, the result of infectious hepatitis. It was their contention that the pregnancy should be terminated in the former, if the general nutrition of the patient was poor, until more information is available concerning the etiology of this type of jaundice. Steiner[4] has urged the more frequent use of preoperative liver function tests in order to bring to light more cases of undiagnosed liver disease. In this connection, however, Day and Hellestrand[31] were unable to demonstrate the value of various liver function tests as a means of determining liver damage in the late toxemias of pregnancy. They were forced to conclude from their studies that the tests were of no value.

The lower nephron syndrome has been reported in association with pregnancy by several investigators.[7-16, 27, 28, 30] Young and McMichael[7] first called our attention to the syndrome in the pregnant patient. They contended that trauma to the soft pelvic tissues released a toxic substance which in turn caused renal failure. Young placed special emphasis on abruptio placentae with concealed hemorrhage as the common denominator in the etiology of this syndrome. Tennent and Starritt,[8] from their study of 17 patients with mixed or concealed accidental hemorrhage from premature separation of the placenta, concluded that the 8 fatalities were produced by shock and anemia with consequent renal ischemia and anoxia causing renal failure. They felt the postulation of a toxic factor to be unnecessary and that treatment should begin with the correction of prenatal anemia. Paxson and Golub,[11] in reporting their 6 fatalities during pregnancy, also emphasize the use of whole blood as an immediate measure in treating the lower nephron syndrome in its earliest stage. Sheehan[9] noted that the incidence of abruptio placentae increased with parity and warned obstetricians to be particularly watchful for the appearance of the crush syndrome following such an obstetric accident. He also points out that of all the initial fatalities from abruptio placentae due to shock and hemorrhage, 6 per cent would have died in the puerperium from massive bilateral cortical necrosis, thus emphasizing the need for immediate blood replacement within the first hour. Greenhill[10] emphatically endorses this policy.

In 1941 Bratton[7] first reported anuria following abortion. He noted 8 fatalities occurring in women with septic abortions who received no blood transfusions. The renal lesions were identical with those found in the crush syndrome. From this Greenhill[7] and others[12-15] have recommended early evacuation of the uterus in all cases of nonseptic abortion associated with oliguria and in all cases of septic abortion as soon as operation is feasible.

Burt and co-workers[17] reported two cases of lower nephron nephrosis following transfusion reactions with survival of both patients and stressed the importance of conservative management with individualization of electrolyte balance in each case. Lucké[27] also has stressed the importance of transfusion reaction as a cause of this condition but includes other causes such as abruptio placentae with concealed hemorrhage,[7] septic abortion,[7, 12-15, 28] toxemia of pregnancy,[18, 27] and hemorrhage from other causes.[11, 16, 27, 28] Trueta and his group[29] have constructed a fairly strong case for the existence of a dual circulation in the kidney parenchyma that, when certain conditions obtain, will provide a shunt of the majority of blood away from the cortex as a protective measure to conserve body fluids. An abnormal persistence of this mechanism could conceivably cause the lower nephron syndrome.

Once the syndrome has become established, regardless of the underlying cause, it is best managed conservatively, as emphasized by several investigators.[11, 15-17, 19, 20, 22, 28] Priddle and Stevenson[19] reported 5 cases of acute renal insufficiency all treated conservatively during the anuric and oliguric phase. One patient failed to survive and autopsy revealed severe bilateral cortical

necrosis. They contend that prompt blood replacement following the occurrence of obstetric shock will lower the incidence of acute renal insufficiency. However, once it is established, the only treatment that will offer any chance of recovery is conservative replacement of fluids and proper maintenance of electrolyte balance. Strauss[28] in his excellent paper reported the results of treatment of lower nephron nephrosis in 7 patients. He emphasizes the conservative management of the syndrome during the stage of renal insufficiency and stresses the danger of overloading the patient with parenteral fluids thereby producing acute pulmonary edema and death. He recommends replacement of actual fluid loss only and a diet of 100 Gm. of glucose daily until the stage of diuresis is reached, when fluids and electrolytes are then replaced volume for volume as reflected in the urinary output. He warns that hyperkalemia can occur quite rapidly during the anuric stage and cause death and should be cautiously watched for as reflected in changes in the daily electrocardiogram. It is the contention of this investigator that the human organism can be kept alive for four or more weeks in the presence of nonfunctioning kidneys if the above-outlined regime is strictly followed.

It is fairly generally conceded by most authorities[8, 28] that radical measures offer no hope in the treatment of this condition and have been abandoned by the majority of investigators dealing with the problem. The successful treatment of two cases of the hepatorenal syndrome by exsanguination transfusions has been recently reported by Snapper and Schaeffer[21] but the relative merits of this method cannot be accurately evaluated until more cases have been reported in the literature. The artificial kidney may well prove to be lifesaving in certain cases but is at present not available in sufficient quantity to be of practical benefit.[24] Certain foreign investigators[20] have attempted to operate upon certain of their patients in the anuric stage without any success and this is mentioned only to be condemned.

The following case is reported in detail because it affords a wealth of information for teaching purposes. Although the major portion of the case is concerned with the management of renal insufficiency in the lower nephron syndrome, it affords ample opportunity to observe the degree of damage that occurs in the livers of these patients who have been subjected to hemorrhagic insults of one kind or another and in our opinion places a great deal of emphasis on the major role played by the liver in such cases. It is for this reason we decided to present the case for your consideration.

CASE 1.—S. N. F., a 27-year-old white dependent wife, gravida iv, para i, abortus ii, with an estimated date of confinement of March 29, 1951, was first admitted to this hospital on Jan. 11, 1951, with the complaint of painless vaginal bleeding. The prenatal course had been entirely uneventful to date and physical examination on admission failed to reveal any hypertension, proteinuria, or edema. The uterus was noted to be just above the umbilicus and the fetal heart was audible at 130 in the lower midline. Blood pressure on admission was 130/54. Vaginal examination was negative for placenta previa. After a few days of bed rest with gradual ambulation followed by no bleeding, the patient was discharged on Jan. 20, 1951, to her home with the diagnosis of partial premature separation of the placenta now quiescent. On Jan. 22, 1951, she had a recurrence of the vaginal bleeding and was admitted to a neighboring military hospital for treatment and disposition. According to their record of the case she was placed at bed rest, blood typed and crossmatched, and she was given sedation and observed carefully throughout the day. About 5 P.M. on January 22, the day of her admission, she had a sudden massive vaginal hemorrhage and promptly went into a state of shock. She received 4 units of plasma, 2,000 c.c. of glucose and water, and a 500 c.c. whole blood transfusion was started. After approximately one-half of the transfusion had run in, the patient developed an elevation of temperature and a chill but the blood was continued regardless as it was considered vital to her treat-

ment. She apparently improved and for the next 24 to 36 hours was observed very carefully. Blood pressure and urinary output were reported to be within normal limits. Labor began about 6 A.M. on January 24, and there was some moderate bleeding present between each contraction. At 8.45 A.M. on Jan. 24, 1951, a premature white stillborn female infant was born spontaneously. The infant was noted to have several congenital defects: bilateral harelip and cleft palate, left clubfoot, and abdominal ascites, and a ruptured encephalocele. Blood loss was estimated as minimal but it was deemed advisable to give more blood and after she was returned to her room another 500 c.c. blood transfusion was started. Again, after approximately 250 c.c. had run in, the patient developed a rise in temperature and a rapid pulse. The transfusion, however, was allowed to run in completely. The immediate postpartum course was uncomplicated and the general condition of the patient was reported as good. There was no impairment of urinary output noted at any time. However, due to the need for more blood replacement it was deemed advisable to transfer the patient to the neighboring Naval Hospital. This was accomplished on Jan. 25, 1951, about 36 hours following the delivery of the stillborn infant.

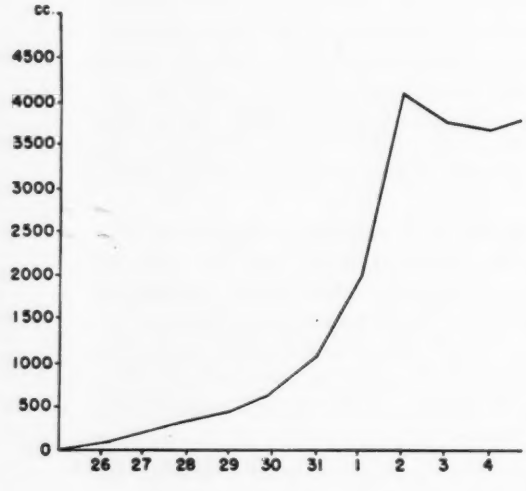

Fig. 1.

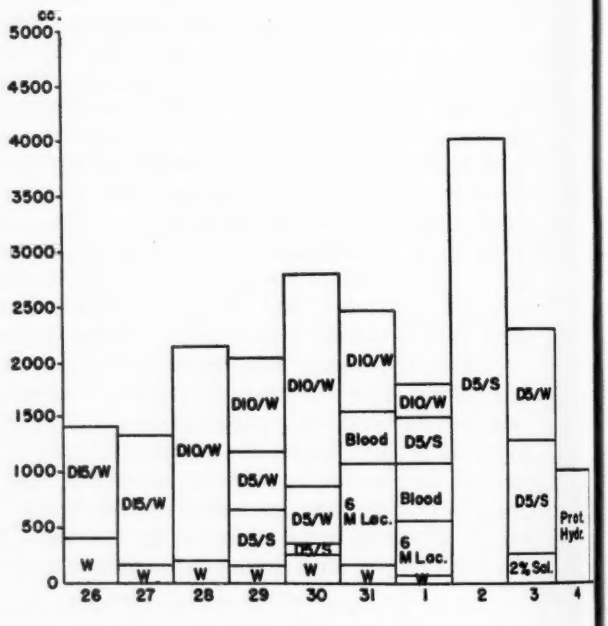

Fig. 2.

Fig. 1.—Total urinary output in hepatorenal syndrome.
Fig. 2.—Fluid therapy in hepatorenal syndrome.

Physical examination on the second admission to our hospital on January 25 revealed a rather ill, icteric appearing, dehydrated, 36 hour post partum white woman. The admission temperature was 100.2° F. and the blood pressure 142/90. The uterus was midway between the umbilicus and symphysis pubis, moderately tender, and well contracted. The abdomen was moderately distended and somewhat tender to palpation. The liver edge could just be felt and was moderately tender. No active vaginal bleeding was noted and the remainder of the physical examination was within normal limits. An emergency blood count was reported as 2,180,000 red blood cells, 45,700 white blood cells, and 7.5 Gm. hemoglobin. An emergency catheterized urine specimen contained 300 mg. per cent of quantitative albumin, was of a deep port-wine color, and was loaded with both red and white blood cells. An icterus index was done and reported to be 62.8 units. The patient was placed in bed, given mild sedation, supported with oxygen, and preparations were made to replace her acute blood loss with whole blood. She passed a fairly uneventful and comfortable night and the morning temperature and pulse were noted to be 100.2° F. and 100, re-

spectively. However, she failed to excrete but 120 c.c. of grossly bloody urine since the time of her admission a little more than 12 hours previously. In view of the renal shutdown that was becoming apparent for the first time since the occurrence of the obstetric accident and two possibly incompatible transfusions, it was the examiner's opinion that a severe lower nephron nephrosis was now present. Postpartum toxemia was also considered quite possible following in the wake of the abruptio placentae. The icterus was thought to be due to intravascular hemolysis either from incompatible blood or from some toxic substance that may have been liberated at the time of the obstetric accidental hemorrhage.[7] The cardiac reserve, however, appeared to be adequate and the lung fields were noted to be clear.

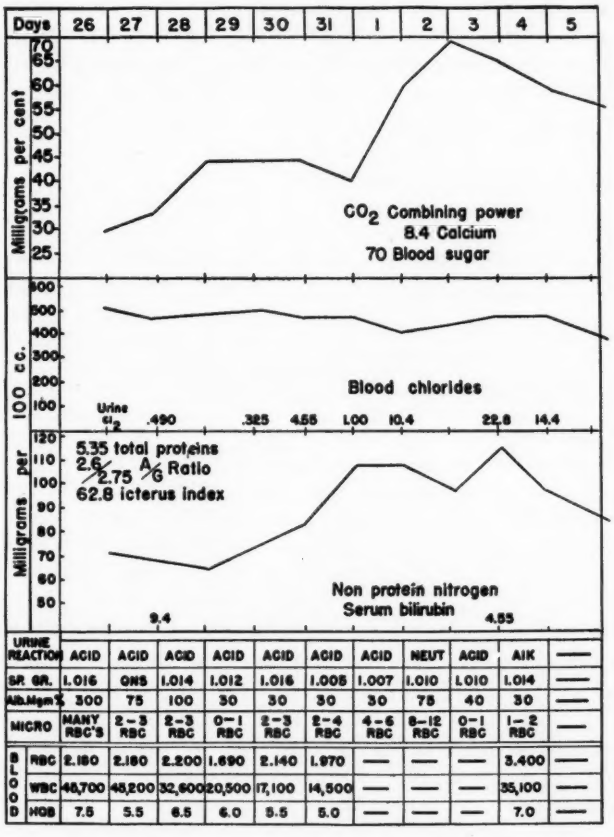

Fig. 3.—Essential laboratory data in hepatorenal syndrome.

The case was managed conservatively by restricting fluid replacement to the insensible loss plus any urine, emesis, or stool output during the preceding 24 hours; by maintaining proper electrolyte balance through replacing chlorides in accord with the rise or fall of blood chlorides, urinary chlorides, and carbon dioxide combining power determinations. Adequate antibiotic therapy was instituted (penicillin and streptomycin in established dosages). Adequate medical consultation was obtained and it was recommended that whole blood transfusions be given as reflected by the level of the daily blood counts but only if considered warranted in view of the already damaged kidneys. Daily essential blood chemistry determinations were obtained and a close watch was kept on the patient's intake and output. Reference to Fig. 1 will reveal the entire urinary output of the patient during her hospital stay. Reference to Fig. 2 will reveal the fluid therapy received by

the patient during her entire hospital stay. Fig. 3 summarizes the essential laboratory data from day to day and to prevent unnecessary repetition will not be quoted in the text. Under this method of management, the patient's clinical condition steadily improved. On the ninth postpartum day she had reached the stage where she was removed from the oxygen tent and it was uppermost in her mind as to when she would be allowed to go home. Suddenly about 1 A.M. on Feb. 2, 1951, she was taken with a convulsive seizure that lasted several minutes and was described by the attending physician to be Jacksonian in type beginning with the left hand and left leg and then becoming generalized. These convulsions could be controlled only by the use of intravenous barbiturates. Prior to the onset of the convulsions the jaundice was almost imperceptible; now it was much more prominent and an acutely tender liver was palpable 4 to 5 fingerbreadths below the right costal margin. The etiology of the convulsive seizures was discussed and salt depletion was thought at first to be the cause and an attempt at adequate replacement with chlorides was made. Potassium imbalance was also considered but was never reflected in the electrocardiographic tracings taken throughout the hospitalization or at the time of convulsions. A spinal puncture was done, the fluid was noted to be clear, and there was no increase of spinal fluid pressure. The patient had in the meantime been returned to the oxygen tent and her general condition was extremely poor. Despite all attempts throughout the following 48 hours at controlling the convulsive seizures, they persisted and became more frequent. The patient's course continued steadily to deteriorate and her general clinical picture became very critical. She slipped into a state of irreversible shock, became deeply comatose, and death was anticipated by only a few hours. About this time tyrosine crystals were reported to be present in the urine on one occasion. Despite all therapeutic measures used, toward midnight on February 4 the temperature began to rise steadily and the pulse and blood pressure began to fall. Death finally ensued at 4:32 A.M. on Feb. 5, 1951.

Pathology Report.—

Liver: Sections show a severe serous hepatitis with the liver cords exhibiting a "moth eaten" appearance with vacuolization in the subendothelial areas of the sinusoids. There is a diffuse necrosis of liver cells, which is most severe in central areas but which is also present toward the periphery of the lobules. Inflammatory cells are not numerous but those present are both polymorphonuclears and lymphocytes. There is some increase in bile within the ductiles (Fig. 4).

Kidneys.—Sections show the glomeruli to be enlarged, relatively bloodless, and to exhibit a rather marked endothelial proliferation. The most striking changes are in the tubules where the great majority of the epithelial cells show loss of nuclei and granular vacuolization of the cytoplasm giving, alternately, the appearance of sucrose and colloid nephrosis. In the interstitial areas there are focal collections of lymphocytes and plasma cells. Also present are small areas which apparently represent infarction with hemorrhage into necrotic parenchyma. In the collecting tubules there are numerous varied-sized masses of lightly brown-staining pigment. The mucosa of the pelvis, in several areas, is denuded (Fig. 5).

Pathologic Diagnosis.—1. Serous hepatitis, severe. 2. Lower nephron nephrosis.

Comment.—This case was reviewed in detail by the Committee on Maternal Welfare of the State of North Carolina.[22] They felt it to be a preventable death on the basis of having started with symptoms of a mild pre-eclampsia. However, we were never able to make a diagnosis of toxemia at any time prior to the actual separation of the placenta as there had never been any proteinuria, hypertension, or edema demonstrable during the prenatal course. Although more than 50 per cent of all cases of abruptio placentae are thought to be preceded by toxemia, it must not be forgotten that there are other precipitating factors active in the production of this obstetric accident.[32] We do not feel that any evidence of toxemia was manifest in this patient while she was in our hospital on the first occasion, and, therefore, it did not make its

Fig. 4.

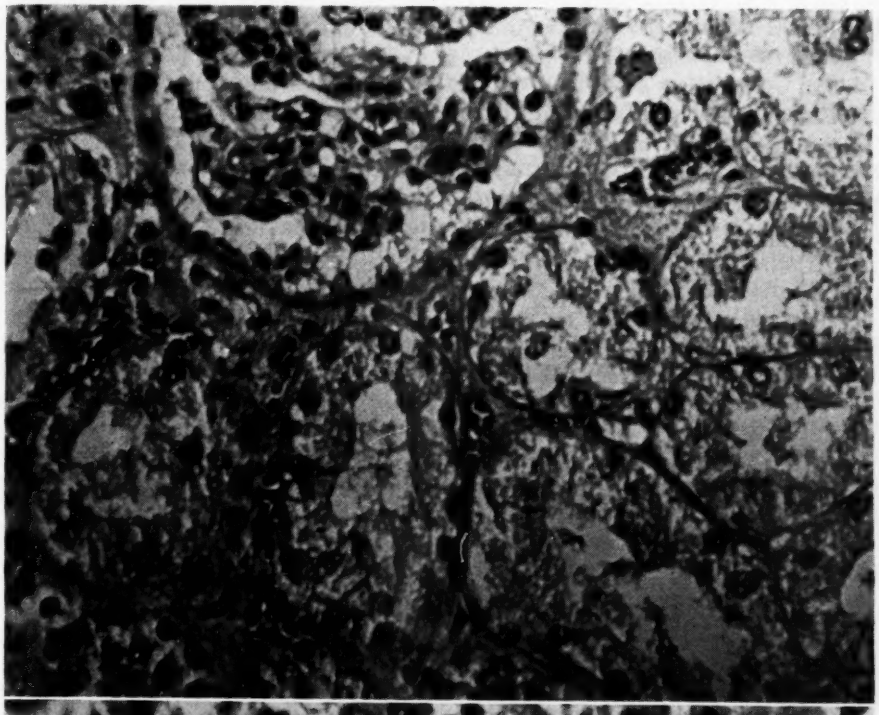

Fig. 5.

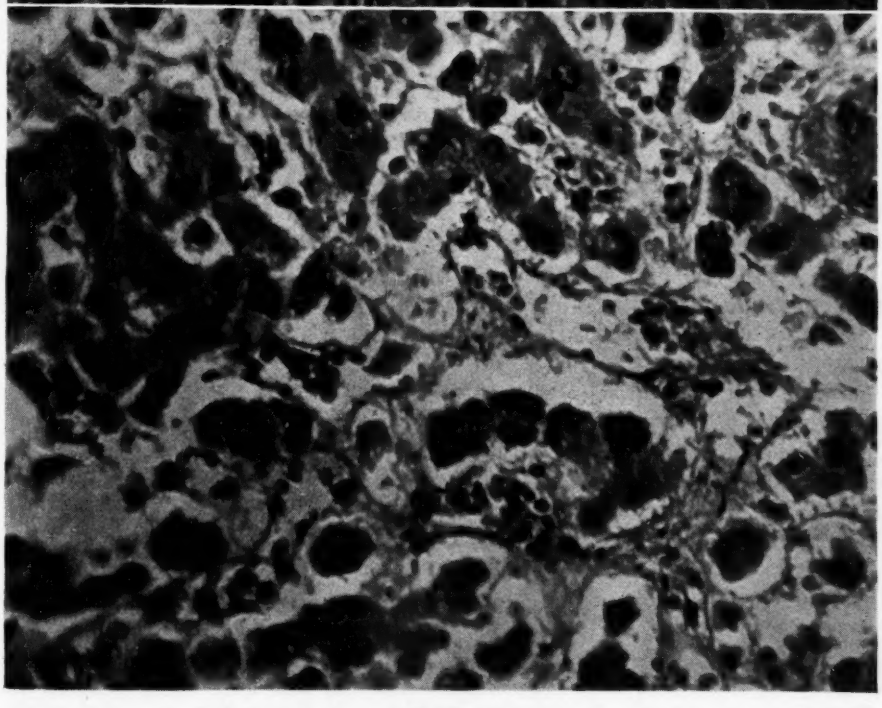

Fig. 4.—Kidney pathology in the hepatorenal syndrome (lower nephron nephrosis).
Fig. 5.—Liver pathology in the hepatorenal syndrome.

appearance until after delivery. An inspection of the case history will dispel any doubts concerning this fact. If a toxemia was present in this case prior to the actual separation of the placenta it must have been of an incipient variety that gave no sign of its presence. Under the circumstances we could not accept the Committee's contention that the death was preventable and directly resultant from unrecognized or improperly managed pre-eclampsia.

The management of the lower nephron syndrome was, however, considered to have been intelligently planned and effectively executed. Our regimen was strictly conservative as recommended by Strauss[28] and other present-day investigators.[2, 8, 11, 13, 16, 17, 19] The essential features were the limiting of fluid replacement during the stage of renal insufficiency to the insensible loss plus that which was lost in urine, stool, and vomitus every twenty-four hours; the rigid maintenance of electrolyte balance; and the affording of a daily diet of at least 100 Gm. of glucose because of its protein-sparing action.[28] When the stage of diuresis began, fluid was replaced volume for volume and electrolytes maintained in balance by careful estimation of 24 hour urine specimens for their chloride content and giving sodium chloride as part of the daily fluid requirements as indicated. Reference to Table I will reveal a summary of the pathology, clinical findings, and suggested outline of treatment of this syndrome.

As undoubtedly noted, our blood replacement in this patient was quite inadequate as judged by modern standards. Certainly the acute anemia must

TABLE I. SUMMARY OF PATHOLOGY, CLINICAL FINDINGS, AND TREATMENT IN THE LOWER NEPHRON SYNDROME

STAGE	DAYS	THE KIDNEY	THE PATIENT	THE TREATMENT
I. Injury	0-1	A. Anoxia of distal convoluted tubules B. Degeneration and focal necrosis of distal convoluted tubules C. Rupture of tubulovenous connections and venous thrombosis D. Precipitation of pigment casts in lower nephron tubules E. Interstitial edema	Hypotension Anemia	1. Whole blood transfusion to replace blood loss and restore blood pressure to normal level (Sympathetic paravertebral block?)
II. Insufficiency	2-14	F. Desquamation (beginning regeneration epithelium fifth day)	Anuria a. Azotemia b. Proteinuria c. Low sodium d. Hyperkalemia e. Hypertension	2. Restrict fluids to output. 3. Maintain Na (6 molar lactate) 4. Give Ca gluconate if acidotic 5. Give high carbohydrate diet or 100 Gm. intravenous glucose daily
III. Diuresis	5-14	G. Regenerated epithelium functional	Diuresis a. Salt loss b. Water loss c. Hypokalemia d. Nitrogen loss	6. Replace urine output volume for volume with normal saline
IV. Convalescence	14-42+	H. Complete healing	Normal renal function	Resume normal diet and fluid intake

be completely and immediately replaced by compatible whole blood regardless of the stage of nephrosis present.[8] Our reticence in initiating earlier blood replacement was based on fear of further damaging already seriously traumatized kidneys. This concept we now admit is unphysiological but at that time it was considered to be the safest method of management.

We feel, as do others,[8, 28] that radical measures to initiate diuresis are unphysiological in their action and may be detrimental to the final outcome and, therefore, should not be used. Some success has been reported with the use of the artificial kidney in these cases. However, even this heroic measure will not combat irreparably damaged kidneys.[24]

The etiology of the lower nephron syndrome has been adequately reviewed by Lucké.[27] Among other causes he lists transfusion reaction, toxemia of pregnancy, septic abortion, and abruptio placentae with concealed hemorrhage. This case was probably caused by the abruptio placentae with hemorrhage and two incompatible blood transfusions. The remote possibility of toxemia is of course a probable cause but, as noted earlier, must have been of the incipient variety as no signs of toxemia were ever present during the prenatal course.

The liver lesions apparently resulted from tissue anoxia sustained during the initial hemorrhagic insult and so impaired the patient's liver function that she was unable to survive.[3] This is indeed concrete evidence of the importance of immediate adequate blood replacement in all cases of obstetric shock from accidental hemorrhage as recently emphasized by Sheehan[9] and Greenhill.[10]

The convulsive seizures that appeared suddenly following the stage of diuresis and remained practically constantly till the death of the patient have successfully eluded logical explanation. Potassium depletion was considered but was never reflected in the electrocardiograms taken during the seizures.[28] Blood calcium and sugar estimations were done and found to be normal. Chloride depletion was also considered but ruled out by blood and urinary chloride values being within normal limits. Spinal puncture was done and the fluid was clear and the pressure was normal. All other possible causes of convulsive seizures were, we believe, considered and effectively ruled out.

The autopsy findings in this case supported the clinical impression of lower nephron nephrosis and acute hepatitis and can be properly considered as findings compatible with the clinical hepatorenal syndrome.[25, 26]

This case was considered to be important from the standpoint of management. It emphasizes the necessity of the obstetrician's maintaining a constant vigilance for the recognition of the most incipient forms of toxemia and the need of an adequate antitoxemia program being a major part of every prenatal clinic.

It also focuses our attention on the critical need for immediate adequate blood replacement in all cases of obstetric hemorrhage. All vital organs apparently undergo some tissue necrosis due to the anoxia resultant from the hemorrhagic insult but the kidneys and liver undoubtedly suffer irreparable damage at times that is incompatible with the maintenance of life.[3, 9]

We hope this case presentation will enliven the interests of both obstetricians and internists to the point where they will be ever cognizant of the devastating sequelae that can result from any accidental hemorrhage occurring in obstetrics and will thereby cause adequate precautions to be taken by all who bear the responsibility for the safe conduct of labor and delivery.

Grateful acknowledgment is made to the Photographic Department of the Naval Field Medical Research Laboratory, Camp Lejeune, N. C., for their help in the preparation

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ENDOSCOPY IN GYNECOLOGY

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THE gynecologist by training, background, and experience is motivated toward the specific and definitive recognition of disease entities as they affect the female pelvis. Diagnoses which are vague and all encompassing such as "pelvic tumor," "surgical abdomen," "menometrorrhagia," and the like are avoided whenever possible. Toward this end, one seeks to perfect oneself in the knowledge of gynecological histopathology, the usual and unusual pathogenetic processes affecting the pelvic viscera, the factors associated with and influencing the incidence of specific types of pelvic disease, and the relation between unconscious mental processes and pelvic symptomatology. In this era of surgical safety and coincident surgical excesses, the gynecologist is particularly well qualified to protect the female patient from ill advised and unnecessary surgical procedures both by himself and by others. Major abdominopelvic surgery is undertaken, in most instances, only after careful evaluation of the patient and her symptoms, repeated pelvic examination, and the utilization of all diagnostic aids necessary and available to arrive at the specific pathologic process operative in the case at hand. Thus, any tool which offers assistance in the determinate identification of the single or major pelvic disease is rapidly accepted in the gynecological armamentarium. Our experience leads us to believe that the culdoscope and the peritoneoscope are such tools. This report represents an analysis of two series of cases; one group of 161 patients studied by two of us (B. V. M. and W. A. R.) using the culdoscope, the other of 30 cases studied by peritoneoscopy (A. R. K.).

Culdoscopy

A complete description of the culdoscope and the technique of its use can be found in the publications of Decker, the originator of the method, and others. To us, any modifications which increase the complexity of its utilization are undesirable. It has been used in all of our cases in the examining room of the gynecological ward. In no instance has general anesthesia been used. When the trocar failed to enter the peritoneal cavity, no attempt was made to enlarge the procedure by isolating and incising the peritoneum under direct vision. Only minimal surgical precautions have been employed. These include, for the most part, the utilization of sterile instruments, the preparation of the vaginal vault with a suitable antiseptic, and the wearing of sterile gloves. Properly selected doses of Nembutal (0.2 Gm.) and Demerol (100 to 125 mg.) as premedication, in combination with 5 to 10 c.c. of 1 per cent procaine for local infiltration of the vaginal vault, have produced adequate anesthetic conditions for the procedure in the majority of the cases. In a few instances the premedication was inadequate and intraperitoneal culdoscopic visualization was con-

tinued in spite of the patient's protests. Our series included examinations performed by our residents and staff under the supervision of the senior author. In every case the intraperitoneal findings were viewed by multiple examiners including medical students acting as clinical clerks on our service. In this fashion a procedure, which can after a little experience be accomplished successfully in 15 minutes, was extended in some instances to 45 minutes. The knee-chest position can become quite tormenting in that length of time.

Culdoscopy has been performed in all instances without the use of special tables, leg holders, straps, etc. The regular gynecological examining table was used. The head of the table was elevated slightly to prevent forward sliding of the patient. She was placed in the knee-chest position and supported by the single assistant whose duty it was to maintain traction on the speculum elevating the perineum.

Technical Results

From May, 1949, to September, 1951, 161 patients have been subjected to culdoscopy as indicated in Table I. In 139 cases, or 86.3 per cent, the culdoscope entered the peritoneal cavity through the vaginal vault with ease. In an additional 11 cases some difficulty was encountered but ultimate success was attained by changing the direction of the trocar or by attempting puncture in a second area. In 11 cases we were unable to enter the peritoneal cavity. No attempt was made to isolate and incise the mobile peritoneum in these instances. Of the 150 cases in which the culdoscope was successfully placed in the peritoneal cavity, the pelvic viscera were clearly and completely visualized in 119 cases. In another 22 cases the visualization was incomplete, yet adequate to identify the disease process present. Thus, in 87.6 per cent of all cases studied, culdoscopy was successful. In nine cases, although entrance was possible, the presence of adhesive bands or the immobility of the uterus or adnexa made adequate visualization for positive diagnosis impossible. We have, therefore, had a failure rate of 12.4 per cent.

Table I. Technical Results

	NO. OF CASES	PER CENT
Total cases	161	
Entered with ease	139	86.3
Entered with difficulty	11	
Well visualized	119	87.6
Adequate visualization	22	
Poor visualization	9	12.4
Failed to enter	11	

Culdoscopic Diagnoses

Table II enumerates the diagnoses established by culdoscopy. As indicated there were 7 cases of ectopic pregnancy. None manifested symptoms of shock and other symptoms associated with acute massive intraperitoneal hemorrhage. All were suspected to be ectopic pregnancies only in so far as every case presenting the triad of menstrual aberration, abdominal pain, and tender adnexal mass is suspected to be a "chronic" ectopic pregnancy until proved otherwise. All were demonstrated at culdoscopy and treated by laparotomy. In one instance the culdoscopist interpreted the visualized pathology as an unruptured tubal pregnancy. Laparotomy established the correct diagnosis of chronic salpingitis. As noted in the table there were 60 cases in which chronic salpingitis was definitively shown to be the pathology producing symptoms. In another 6 instances chronic salpingitis was found, but was not

the factor producing the symptoms necessitating the patient's hospital admission. The outpatient and ward services of large hospitals present a never-ending stream of patients whose recurrent Neisserian infections present the manifestations of tubal pregnancy and whose tubal pregnancies can quite easily be neglected in the diagnosis of pelvic inflammatory disease. For this reason chronic salpingitis was the most frequent lesion detected.

TABLE II. INTRAPERITONEAL PELVIC DISEASE

DISEASE	NO. SYMPTOMATIC	NO. ASYMPTOMATIC
Ectopic pregnancy	7	—
Chronic salpingitis	60	6
Endometriosis	6	9
Leiomyomas	8	10
Postoperative adhesions	8	2
Ovarian neoplasms	3	—

Pelvic endometriosis was identified as the specific cause of the patient's pain in six cases. In another nine cases minimal areas of endometriosis were seen on the ovaries, tubes, and pelvic peritoneum which had been entirely unsuspected or were obviously not factors in the patient's symptomatology. Eight symptom-producing uterine leiomyomas were identified. Subsequent laparotomy confirmed the diagnosis. Small incidental fibroids were found in 10 instances. The patient's symptoms were identified as due to postoperative adhesions in 8 cases and such adhesions were interpreted as being coincidental in another two cases.

Three adnexal neoplasms were seen. Of these, laparotomy proved one to be a Brenner tumor, the second to be a parovarian cyst, and the third a dermoid. In the case of the Brenner tumor, the culdoscopist described the ovarian neoplasm as solid and "fibrotic" in appearance. The parovarian cyst was identified as a cystic ovarian neoplasm. The dermoid was thought to be a dermoid cyst.

As demonstrated in Table III there were 32 cases in which the uterus, tubes, and ovaries were completely normal. In three cases nonneoplastic physiological cysts of the ovary could be identified as the cause of the patient's complaints. In an additional 15 cases physiological ovarian cysts were identified but did not contribute to the patient's symptoms. Six cases were ultimately classified as incomplete abortions and two as normal intrauterine pregnancy.

TABLE III. NO INTRAPERITONEAL DISEASE

DIAGNOSIS	NO. OF CASES
Normal pelvis	32
Physiologic ovarian cysts	3
Incomplete abortion	6
Uterine pregnancy	2

Special Studies

In this series, culdoscopy, as indicated in Table IV, enabled us to rule out an ectopic gestation in 54 cases. The subsequent clinical course and in a few instances laparotomy confirmed the culdoscopic interpretation. In 6 cases of postmenopausal bleeding, the possibility of an intraperitoneal pelvic malignancy was excluded. Three cases subsequently seen by the psychiatric consultant and managed as cases of anxiety hysteria were shown to have no intraperitoneal pelvic pathology to account for or contribute to their bizarre pelvic symptoms.

In six instances where infertility was a prominent complaint, the culdoscopist was able to evaluate the presence or absence of pelvic pathology. Studies for infertility and tubal patency were not a significant part of this series. In three instances methylene blue was injected into the cervical canal and the dye could be seen emerging from the fimbriated extremities of the tubes. In these instances the procedure was performed for purposes of familiarization and not for specific studies. As our use of the instrument continues, it is planned to utilize this method in those cases of female infertility where plastic procedures are contemplated for the correction of tubal abnormalities.

TABLE IV. SPECIAL STUDIES

DIAGNOSIS	NO. OF CASES
Ectopic pregnancy ruled out	54
Postmenopausal bleeding	6
Anxiety hysteria	3
Infertility	6
Tubal patency	3

Of the 161 cases, 47 came to subsequent intraperitoneal surgery. In 46 instances the operation was abdominal and in one vaginal hysterectomy permitted direct visualization of the tubes and ovaries. In 41, the findings of the culdoscopist were completely confirmed. The 6 cases in which the culdoscopic interpretation was impossible or inaccurate indicate some pitfalls and inadequacies inherent in the method and others attributable to inexperience on the part of the examiner. Three of these cases have been classified as poorly visualized (Table I). Laparotomy demonstrated that the scope had entered the peritoneal cavity and that visualization was impossible because of extensive pelvic inflammatory pathology with adhesions. In one instance the pelvis was well visualized and no adhesions were identified. However, at laparotomy the surgeon found extensive adhesions of bowel and adnexa above the cul-de-sac. During the early part of this series one case was described as showing minimal bilateral tubal changes due to inflammation and laparotomy demonstrated tubes that were grossly normal. The major error in interpretation occurred in the single instance where the culdoscopist made a diagnosis of unruptured tubal pregnancy in the case which at prompt laparotomy proved to be inflammatory disease.

Complications

That culdoscopy, in our hands, is not a completely innocous procedure is demonstrated by Table V. In practically all instances where the instrument entered the peritoneal cavity some shoulder pain and minimal abdominal discomfort followed. In those cases where nothing could be visualized and the peritoneum was thought to have remained intact, the manifestations of pneumoperitoneum indicated that pathology rather than failure to puncture a moving peritoneum precluded visualization. The symptoms produced by residual intraperitoneal air are not considered a complication.

TABLE V. COMPLICATIONS

Rectal perforations	2
Pelvic peritonitis	5
Pelvic peritonitis with abscess	1
Vaginal wound hemorrhage	2
Hematoma with abscess	1
Total	11 (6.8 per cent)

As noted there were two cases of perforation into the rectum. In the first case we were so alarmed that immediate laparotomy was performed. The lesion was found to be retroperitoneal and in spite of the fact that the posterior peritoneum was opened to repair the defect in the rectal wall the patient's postoperative course was fortunately without untoward incident. In the second instance of rectal perforation, no treatment was instituted and the patient manifested no symptoms of illness.

Symptoms and signs of pelvic peritonitis followed shortly after the completion of six cases. In five, all symptoms subsided within 48 hours and after treatment with penicillin. In one case, abscess formation occurred requiring incision and drainage before recovery. All of these cases were early acute exacerbations of chronic salpingitis in which the technical procedure probably precipitated the peritonitis. Two cases of vaginal wound hemorrhage were encountered. These required packing to control the excessive bleeding. One hematoma became infected and required drainage of the abscess. At no time were any of these patients seriously ill. There was no mortality.

Peritoneoscopy

During this study there were 30 cases in which the peritoneoscope was employed. The technique followed that recommended by Ruddock. Premedication with suitable doses of Nembutal, morphine sulfate, and novatropine was employed. One per cent procaine was used for local infiltration of the abdominal wall at the site of puncture. All procedures were performed in an operating room and all surgical precautions were maintained. The Trendelenburg position was used.

Table VI indicates that, of the 30 cases studied, there were 4 failures, or a rate of 13.3 per cent. In 3 visualization was inadequate. In one the findings were inaccurately interpreted as evidenced by subsequent laparotomy. By this method we were able to establish the diagnosis of ectopic pregnancy in two instances and in one instance each of ovarian malignancy and tuberculous salpingitis. Three suspected cases of endometriosis were confirmed. In 16 cases suspected ectopic pregnancy was ruled out. Suspected endometriosis and tuberculous salpingitis were ruled out in two cases. There were no complications resulting from the peritoneoscopic investigations.

TABLE VI. PERITONEOSCOPY

	NO. OF CASES	PER CENT
Total	30	
Failures	4	13.3
Ectopic pregnancy	2	
Ectopic pregnancy ruled out	16	
Endometriosis	3	
Ovarian neoplasm	1	
Tuberculous salpingitis	1	
Complications	0	

Comment

This study indicates that both the culdoscope and the peritoneoscope can be valuable aids in gynecological diagnosis. Culdoscopy is a more convenient method. The advantages of a procedure which does not require the use of an operating room, which avoids the dangers of general anesthesia, which can be performed with few and simple tools, and which requires only one unskilled assistant, are self-evident. Peritoneoscopy is of particular value in those cases where culdoscopy cannot be accomplished or is contraindicated. Patients con-

sidered unsuitable for culdoscopy include those who present a very small introitus, a markedly inflamed and tender vagina, or a fixed cul-de-sac mass. In addition, patients unable to maintain the knee-chest position because of physical or psychological difficulties are preferably studied by peritoneoscopy.

It has been our experience and that of others that the manifestations of tubal gestation are so protean as to humble the most alert of gynecological diagnosticians. When outpatient clinics are under the supervision of changing personnel and individual members of the clinic population are somewhat inarticulate in describing the sequential events of their "misery," errors of omission and commission relative to tubal gestation are inevitable. We have sought to maintain a high index of suspicion among all members of our staff but, in spite of this, occasional instances of repeat clinic visits have occurred before the true diagnosis was dramatically demonstrated by the unexpected occurence of severe intra-abdominal hemorrhage and its associated findings. In order to minimize such occurrences, we have established the policy of admitting all cases which in any way suggest the possibility of eccyesis to our wards for observation until such time as a definitive diagnosis can be established with safety.

Prior methods of study have been, for the most part, satisfactory but not always without significant error. Patients under observation in the hospital have had initial or additional intraperitoneal hemorrhages during the night hours and the recognition of the serious nature of their condition has been delayed. Biologic tests for pregnancy, cul-de-sac punctures and observations of hematocrit progress have occasionally been disappointingly inaccurate in establishing the correct diagnosis. At times the diagnosis of tubal pregnancy seemed established by the findings and laparotomy failed to demonstrate it. Such observations have, in addition, consumed many hospital days and have contributed to the financial burden of both the patient and the hospital.

We find it difficult to attain a high level of accuracy in the diagnosis, based on history and pelvic examination, of endometriosis. We do not hesitate to choose abdominal surgery for those women whose age exceeds 35 years and whose pelvic examination reveals palpable pathology. However, in the younger age groups, where the symptoms and pelvic findings are merely suggestive, we seek to defer the surgical approach for as long as possible. With the advent of androgenic and estrogenic therapy, the problem has become even more complex. We are especially interested in the use of progressively increasing doses of stilbestrol in the conservative medical management of endometriosis in the young woman. Since relief of symptoms after use of these measures may often open to question the original diagnosis of endometriosis, we have found endoscopy a useful method of establishing a diagnosis objectively.

In other cases presenting the clinical history of acquired progressive dysmenorrhea, there have been no abnormal pelvic findings, and endoscopy has enabled us to rule out endometriosis. In some instances where pelvic findings of firm, fixed masses and palpable tender nodules seem to establish the cause of pelvic pain, culdoscopy or peritoneoscopy demonstrated that the lesion was chronic bilateral salpingitis rather than endometriosis.

In the postmenopausal patient, pelvic examination is frequently unsatisfactory. Since the detection of serious tubal and ovarian neoplasms may depend entirely on routine prophylactic pelvic examinations, when these examinations are unsatisfactory or merely suggestive, the patient is subjected to either the hazard of exploratory surgery or the hazard of additional observation. During this period of observation a questionable adnexal mass may advance beyond the point of salvage. In those cases of postmenopausal uterine bleeding where curettage and cervical biopsy combined with pelvic examination under anesthesia failed to demonstrate the cause of the bleeding and where the use of estrogens has not been a masquerading factor, we have grown increasingly prone to enter

the abdomen and remove the uterus, tubes, and ovaries in order to demonstrate the absence of intrauterine, tubal, or ovarian malignancy. In cases where the bleeding seems to be explained by some local benign causes as determined by curettage and cervical biopsy, we have appreciated the additional assurance furnished by endoscopy.

Our work has demonstrated not only the ability of endoscopy to aid in the evaluation of the complaints due to organic disease, but also in assessing psychogenic factors which contribute to the symptom complex. The gynecologist must have the training, experience, and patience to evaluate the psychosomatic aspects of the patient's pelvic complaints. Too often doubt has been resolved by meddlesome surgery. The sequence of repeated abdominopelvic operations in the emotionally disturbed is a commonly observed experience. On the other hand, competent psychotherapeutic approaches have ameliorated symptoms in spite of the presence of undetected progressive malignant lesions. Endoscopy offers an opportunity to rule out or discover a coincident organic intraperitoneal pelvic lesion.

Summary

This report is an analysis of 191 cases in which endoscopy was employed in an effort to establish the correct diagnosis in patients whose symptoms and findings did not unequivocally warrant abdominal surgery. In 87 per cent of all cases studied, we were able to establish the diagnosis by this method. In the remaining 13 per cent of cases, failure to enter the peritoneal cavity or inadequate visualization made positive diagnosis impossible.

The method has proved particularly valuable in the rapid identification of the presence or absence of ectopic pregnancy, chronic bilateral salpingitis, endometriosis, adnexal neoplasms, and pelvic pathology associated with anxiety states. It would appear to be of value in the determination of female factors contributing to infertility.

The incidence of serious complications in culdoscopy was 6.8 per cent. Two rectal perforations occurred early in the series. These, when they occur, are retroperitoneal and should be treated by observation with or without antibiotic medication. The incidence of pelvic peritonitis may have been increased by breaks in technique associated with prolonged viewing by multiple examiners. There was no mortality. It is our belief that the complications were not sufficient in number or extent to preclude the use of the instrument in the manner and under the conditions described. There were no complications following peritoneoscopy.

Endoscopy, in our experience, is of such value, and can be employed with such ease, as to deserve more widespread use among gynecologists.

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PROBLEMS AND DIFFICULTIES IN THE CLINICAL TEACHING OF OBSTETRICS AND GYNECOLOGY AS OF TODAY*

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IN BYGONE years the teaching of obstetrics and gynecology was on a very casual basis. In the early French hospitals the obstetrical patients were usually found in the cellar of the hospital in order to assure privacy, and the whole process of care during labor was conducted in an atmosphere of secrecy. This was the time, too, when it was considered to be highly immoral for the lying-in woman to be seen or attended by a male physician. Obviously, clinical instruction under such conditions was all but impossible.

In Germany, conditions were somewhat better; and when Johann Fried organized the first *Frauenklinik* in Strasbourg in 1730, he utilized the patients presenting themselves for the instruction of medical students as well as midwives.

In this country, the first student course was offered by Dr. William Shippen in Philadelphia in the latter part of the eighteenth century. This was purely didactic with no opportunity for clinical instruction. Not until 1850 was any serious effort made to give the medical student a real clinical demonstration. The pioneer along this line was Dr. James P. White of Buffalo, who in that year conducted a delivery before the graduating class of Buffalo Medical School. What a truly pioneer effort this was was indicated by the effects that this innovation produced. The students appreciated the effort that Dr. White had made on their behalf, but Dr. White suffered the fate of so many pioneers in being vilified by the public, the press, and even by his own colleagues.

From that time on, progress in clinical teaching went on, but so very slowly. That great teacher, the late J. Whitridge Williams, has told with great glee how at the time of his graduation from the University of Maryland in 1888 he had had the opportunity to observe two deliveries and yet had won the obstetric prize for that year. Graduating some twenty years later my own experience was comparable but slightly better. I observed four deliveries, palpated the abdomen of one pregnant woman at the time of my final examination, never did a rectal or vaginal examination, and never had a pelvimeter in my hands. From what has been said, it is obvious that the clinical teaching of obstetrics in this country was in a sad state up to a fairly recent period. As for the clinical teaching of gynecology, it was almost nonexistent.

Fortunately, however, from the early part of this century, great improvement can be recorded. This improvement coincides with the establishment of

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numerous university women's clinics in many of our university centers. In these clinics serious efforts have been made to give adequate clinical instruction in obstetrics and gynecology, both undergraduate and postgraduate. I believe that the results of such instruction are seen today in the low maternal mortality rate which this country enjoys, as well as the greatly improved results in pelvic surgery. These excellent results have developed notwithstanding the handicaps that the curriculum makers in our schools have at times interposed, and too often the time allotted for obstetrical and gynecological undergraduate instruction is completely inadequate.

In recent years new problems have arisen which are bound to have a profound effect in our educational efforts. As one who has spent some forty-odd years in a teaching career which is now approaching its close, I cannot help but view with considerable alarm some of the trends which are developing and the possible effects which they may have on the clinical teaching of obstetrics and gynecology. I refer in particular to the advent of hospital and surgical insurance to which such a large percentage of our population are now subscribing and receiving the benefits thereof, as well as the changed economic conditions of the country as a whole.

In the past, clinical instructions to students have been carried out practically exclusively by the use of clinic patients. The spread of the various insurance plans, together with changed economic conditions has reduced the number of clinic patients very materially; and if general compulsory insurance should be brought into being, which God forbid, there simply would be no ward patients at all. Does it mean that, with a high percentage of patients falling in the private or semiprivate category, clinical teaching must be abandoned? Not at all, but it does mean that there will have to be striking modifications of present methods; in fact, these modifications have already been inaugurated in many medical centers.

Didactic teaching by lectures, recitations, laboratory procedures, of such subjects as obstetrical and gynecological pathology are of course not affected. It is the clinical teaching which presents the problems. These problems, resulting from the decrease in the number of ward patients, are to a large extent peculiar to obstetrics and gynecology. Internal medicine and pediatrics need hardly be affected at all, but surgery and the surgical specialties are, though to a less extent than is the case with obstetrics and gynecology. Perhaps I can present the factors involved more clearly if I discuss the situation as it presents itself in my own clinic, although, from information obtained from other heads of similar departments elsewhere, the problems are similar in other clinics. The problems involved affect undergraduate instruction and also the training to be offered to those interested in the specialty as a career after graduation. As there are different aspects to the problems as they affect these two groups, they will be discussed separately.

When clinical teaching began in the University of Rochester in 1926, I made it a point to see that students should have just as close contact with obstetrical

and gynecological patients as they had with medical and surgical patients. I have never had reason to regret this move—not exactly an innovation, yet different from the custom in many schools at that time.

Perhaps it would be desirable to outline briefly what we feel are the essentials in undergraduate clinical teaching. Of first importance is an adequate and complete history, and the student should receive meticulous instruction on how to obtain a proper history. Too often the beginner and even the older person tends to be rather casual about this. It should be impressed on the student from the beginning that he should see the patient as a whole and not just pay attention to the problem which has brought her to the hospital. Other equally important conditions may be present and awaiting diagnostic discovery.

In obstetrics the fundamentals of the special methods of physical diagnosis will form the groundwork of elementary instruction, abdominal palpation, pelvimetry, vaginal and rectal examination. The student should observe and assist at an adequate number of deliveries and then be permitted to conduct a proper number of deliveries himself under supervision. He must be instructed in the recognition of complications of pregnancy and abnormalities of labor and be given the opportunity to observe how these abnormal situations are handled. Observation and care of the puerperal woman, both normal and with complications, is also of importance. These points can be covered by the observation of the student on individual patients assigned to him as well as by ward rounds and group discussions. Observation of ambulatory patients in the prenatal clinic of the outpatient department should also form a part of the teaching program. Attendance on lying-in women in their homes by students, when properly supervised, has always been a valuable feature of clinical instruction when it is available.

In gynecology undergraduate clinical instruction should center on adequate instruction in diagnostic methods with opportunity to examine as large a number of patients as possible. Methods of minor therapy, such as office treatments, may be presented in the outpatient department on the ambulatory patient. The student should be made "cancer conscious," so to speak, in the hope that more and more early examples of this dread disease will be detected. I have found, in the gynecological patient who is to be submitted to operation, that examination under anesthesia is of great instructive value. At this time, if a laparotomy be performed, the student has the opportunity actually to see what has felt on examination, confirming his findings or checking his mistakes. Such examinations need not be limited to a single student but may be participated in by a small group on each patient. Gross and microscopic study of material removed at operation will make the clinical story in these patients complete. From the gynecological standpoint, then, in so far as clinical instruction of students is concerned, emphasis should be placed on diagnostic methods and minor treatments including hormone therapy which occupies such an important place in modern gynecological therapy.

While indications for various operative procedures should be presented, the actual instruction in operative technique, except perhaps for biopsy or diag-

nostic curettage, has in my opinion no place in undergraduate instructions. What has been outlined above represents the minimum that should be attempted in undergraduate instruction in obstetrics and gynecology; more would be desirable but is not often attainable.

With an adequate number of patients presenting themselves in a clinic, no difficulty should arise in meeting these standards, but with the present decrease in the number of such patients and the great increase in the numbers of semiprivate and private patients, can such a standard be maintained? Only two alternatives are possible; either to limit clinical instruction to what can be done with the greatly diminished number of ward patients available, thus reducing the clinical instruction to a dangerously low level, or to make use of semiprivate and even private patients for undergraduate instruction to replace the loss of ward material. In my department we have adopted this latter policy and have been carrying it out for several years with reasonable success. On the obstetrical floors each patient on admission is assigned to a senior student who is responsible for the general "work-up" and laboratory studies. He follows the course of events during the labor, and assists the attending physician at the time of delivery. He then follows the patient during the puerperium. To date no patients have offered any serious objections to this line of procedure; on the contrary, many appear to welcome the extra attention they thus receive. Semiprivate patients can be utilized for students' rounds though perhaps not with the freedom of ward patients. Generally speaking, it will be preferable when they are so utilized that the patient's own attending physician should conduct the rounds. The most serious effect of changed conditions so far as the undergraduate student is concerned is the impossibility of providing anything like an adequate number of personal deliveries for him to conduct. In the larger centers, where care of the lying-in woman in her home formerly formed an important feature of undergraduate instruction, circumstances have either necessitated abandonment of this type of instruction or have seriously curtailed it. On the other hand changed conditions have affected dispensary or outpatient material and teaching very little as yet.

We also utilize semiprivate gynecological patients for undergraduate instruction. Each patient on admission is assigned to a fourth-year student for history and general work-up. He follows her to the operating room, examines her under anesthesia, may on occasion assist at the operation and follows her postoperatively. He also has opportunity to study the gross and microscopic pathological findings. This line of procedure has proved to be reasonably satisfactory and furthers our efforts to improve the student's diagnostic ability.

We come now to the problem of the postgraduate training of those individuals who seek training in the specialty of obstetrics and gynecology which they plan to follow as a career. These are the men who will eventually fill the important teaching positions in our medical schools, on the one hand, or who will assume the responsibilities of private practice of the specialty, on the other. It is obvious that their training must be very complete and of a high order.

Consideration must also be given to the training of the man who is planning general practice as a career. In the past few years it has been my observation that an increasing number of men are planning such careers, in my opinion a fortunate circumstance for medicine as a whole. Such men will require a broad training after graduation and such training should include a proper assignment of time in obstetrics and gynecology. This training obviously need not be as extensive as that provided to those who are planning to practice the specialty as a career, but it should include the opportunity to care for an adequate number of obstetrical patients, normal and abnormal, and to become familiar with the simpler obstetrical operative procedures. It should also include opportunity to further perfect himself in gynecological diagnostic procedures, office therapy, and the simple operative procedures, such as biopsy and curettage. The training of these men can be carried out at the intern level concurrently with the early part of the training of those who are planning more extensive training in the specialty as a career.

In the past, the so-called resident system, as carried out in many institutions after the plan originally begun at the Johns Hopkins Hospital, has provided a steady supply of men to fill the various academic posts and to provide an adequate number of highly trained practitioners of the specialty. Under this program an individual progressed from internship to the post of chief resident over a varying period of years, usually at least four or five years. Each succeeding year he was given increased responsibilities in the care of patients, conducted normal and operative deliveries, and was permited to perform many gynecological operations under supervision, beginning with the simple minor ones and progressing by stages to the major operative procedures with which the pelvic surgeon must be familiar.

Present conditions have had a very serious effect on this type of program on account of the great decrease in the number of ward patients who formerly formed the pool of clinical material from which the resident staff obtained their chief experience and training. The young man of course acquires valuable training in observing and assisting experienced operators in their care of private patients, but such limited training can be carried only to a certain point and cannot be regarded as complete. For the final training of a man, he must have the opportunity to exercise his own judgment and to carry out operative procedures of all types himself. After all, a man learns to operate by operating. Under the usual system of resident training his last year of hospital service included this type of work, the chief resident being usually responsible for the operative procedures carried out on the majority of the ward patients. The decrease in the clinical material upon which the resident staff was dependent for their training jeopardizes this program and, with the further extension of insurance of the population, the problem will become still more acute.

The patient who carries hospital insurance and enters a hospital on a semiprivate basis will have practically no hospital charges to meet and will often be in a position to select her own physician and pay a moderate fee for such procedures as may be carried out. If, in addition to hospital insurance, she also is covered

by surgical insurance, she almost certainly will select her own doctor; in fact, one of the conditions of most such insurance policies is that the patient shall have a free choice of physicians. The patient having selected a staff member, can he in fairness turn her over to a resident for delivery or operation? To do this without the patient's consent would seem at least unethical, if not frankly dishonest. If the patient is turned over to a resident for care under the supervision of the attending physician, who should collect the fee involved? Should it go to the attending man who accepted the responsibility, to the resident who performed the operation, or delivery, or should it be shared? One can visualize many disagreeable situations arising in connection with this fee problem.

With these points in mind, what can be done to maintain the resident training program at anything like an adequate level? Unfortunately I have no specific solution to offer for this problem. I have, however, a suggestion or two to offer which may be worthy of thought.

An insurance policy might be offered covering hospital, obstetrical, and surgical care at a lower rate than that currently charged, and made available to persons unable or unwilling to pay the higher rates charged on present policies. Obviously only those in a relatively low income group should be eligible for this insurance. This would represent the group who would formerly enter the hospital as ward patients.

The holders of such policies would enter the hospital without being assigned to a particular physician but rather with the understanding that their care will be carried out by the members of the resident staff, with, however, the important proviso that such care, operative or otherwise, would be supervised by some member of the attending staff assigned to that duty. The medical fees would be smaller than in the case of the usual policy on account of the lower premium charged. These fees could be pooled and then divided among the attending physicians who participated in the supervising program according to the amount of time each one spent on it. This plan should prevent the criticism of a hospital practicing medicine in competition with the private physician. This would seem to be a workable as well as a fair plan by which the patient would receive adequate care, an all important feature of any program, and the jeopardy to the resident training program be at least reduced.

Another alternative would be to return to the preceptorial plan of assistantships so widely employed a generation ago. When in vogue, this plan worked fairly well and is employed in some places today with reasonable success. It has obvious limitations, however, and can never have the generally satisfactory results that we expect from the well-developed resident system which is now endangered.

Still another possibility which could be made applicable to the teaching institution is similar to the first suggestion but on a broader basis. This would be a plan in which all insurance-covered patients are admitted to a group in the hospital rather than to an individual—the patients of course being made to understand that they are being so admitted. One or more members of the attending staff would decide who should care for the patient, whether a member of

the resident staff, a junior or a senior attending staff member, according to the medical needs of the patient rather than the financial standing. Again, the insurance fees would be pooled and distributed on a pro rata basis among the participating members of the group involved. Patients included in this plan or in the first plan should also be available for undergraduate instruction.

This question of the hospital practicing medicine is to some extent at least a result of the inauguration of the so-called "full-time" plan in connection with clinical departments of the medical school. The advantages of such a plan from the standpoint of instruction and investigation are indisputable. On the other hand, those who have assumed such full-time academic duties should not be exploited by the institution. In the handling of this problem only two alternatives are possible, as I see it. First, the individual who selects full-time academic medicine as a career should be paid such a salary as to obviate the necessity of this supplementing his income by fees from patients. In most institutions this would be impossible on account of the money involved. Furthermore, it would tend to seclude the full-time man, and reduce his contacts with his fellows in the profession. The alternative is to pay the full-time man a reasonable salary which may be supplemented by the collection of fees from private patients and retained by him without the institution coming in as a third party in the transaction. This is why I bring up the problem in connection with insurance-covered patients and why I feel that if either of the schemes I suggest were adopted, the fees collected should be distributed among the participating physicians.

Conclusion

I have presented certain problems which have developed in connection with the clinical teaching of obstetrics and gynecology from both the undergraduate and postgraduate standpoints. The problems have arisen largely as the result of changed economic conditions and the extension of hospital and surgical insurance plans. The insurance plans are unquestionably here to stay and will also without doubt be extended still further. Desirable as they are from many standpoints, there is no disguising the fact that they are having a serious effect on medical education. Undergraduate clinical instruction is menaced to some extent but the most serious problem is the jeopardy in which the resident training program is placed. As one interested in such education, I believe the situation is a truly serious one which may well become more acute. The suggestions I have presented to help correct the situation are not ideal, far from it in fact, but are, I believe, worthy of serious consideration. Some means will assuredly have to be developed if our educational training program is not to be further endangered.

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COITUS AND LATE PREGNANCY, DELIVERY, AND THE PUERPERIUM*

A Preliminary Report

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VARIOUS American textbooks of obstetrics are in general agreement that coitus during the last two months of pregnancy is ill advised. Such complications as infection, premature rupture of the fetal membranes, premature delivery, and hemorrhage are described. The subject of coitus as related to late pregnancy, delivery, and the puerperium is absent from the American literature, as listed in the *Index Medicus*, since 1916.

The traditional advice given women by their physicians, to refrain from coitus during the final two months of their pregnancies, evidently stems from the existing outdated, foreign literature.

Koller,[1] in 1936, observed an 8 per cent puerperal morbidity in patients delivered spontaneously, who had not had intercourse 2 weeks or less prior to delivery. He reported a 10 per cent morbidity in patients delivered spontaneously who had had coitus 2 weeks or less prior to delivery. In operative vaginal deliveries the percentages were 31 and 36, respectively. Ruge[2] found a 17 per cent puerperal morbidity in 82 women who had had intercourse during the last 3 days prior to delivery. He also reported 78.5 per cent of his patients as having coitus during the last 2 months before delivery. Schultze[3] notes that Von Beuben was the first to formulate the theory that coitus in the last weeks of gestation predisposes to premature rupture of the membranes. Von Beuben found coitus occurring in 23 per cent of his patients 8 days or less prior to delivery. There was a 29 per cent incidence of premature rupture of the membranes in his series.

So many facets of obstetrical practice have changed so radically since the last contribution to the literature in 1937 that we probably err in clinging to precepts put forth only up to that time.

Here is an analysis of 100 unselected cases admitted to the obstetrical service of Louisville General Hospital between Aug. 6, 1951, and Sept. 7, 1951, intended to stimulate through new perspective, a re-evaluation of our ideas about coitus and late pregnancy.

Material and Methods

Of the 100 patients studied, 25 were primiparas and 75 were multiparas; 63 were Negro and 37 were white. Eighty of the patients were married and 20 were unmarried. The latter group was composed of 11 single women, 6 separated, 1 divorced, and 2 widowed. All patients were studied objectively and subjectively.

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After the admission history and physical examination, a sterile speculum examination of the vagina was done. The posterior vaginal fornix was exposed and a smear made from its secretions. The dried smears were then sent to the laboratory for staining, and examination for spermatozoa. Next, the contents of the posterior vaginal fornix were aspirated with a blunt-tipped, malleable cannula. Fluid thus obtained was placed in 0.5 ml. to 1.0 ml. of normal saline solution; mixed and heated very gently; and examined microscopically for evidence of motile spermatozoa.

Patients were evaluated subjectively by their answers to this question, "When was the last time you had intercourse before coming to the hospital?" which was asked routinely by the admitting resident and again by me on the first postpartum or second hospital day. Answers were prompt, consistent, and in my opinion, as truthful as the patients' memories permitted. Time of the last coitus prior to admission was usually reckoned by the patients in terms of days, weeks, or months. For this study all times have been recorded as days, on the basis of a 7 day week and a 28 day month. In text, figures, and tables, the time of last coitus prior to admission is expressed in days as "time coitus."

Results

Spermatozoa were demonstrated on two occasions in the wet preparations. The dry smears were uniformly negative (Table I). Since the objective search for spermatozoa in the vaginal fluid was 98 per cent negative, "time coitus" comes to the fore as the pertinent factor here reported.

TABLE I. ASPIRATION OF POSTERIOR VAGINAL FORNIX, 100 CASES

PREPARATION	WET	DRY
Spermatozoa	2	0
No spermatozoa	98	100
Total	100	100

Shortest average time coitus prior to admission (Fig. 1) was reported by white married multiparas; longest time average, by white unmarried primiparas. Except for Negro primiparas, in each corresponding group as to race and parity, as well as in the averages as to marital status, married women averaged the more recent time of intercourse. These results undoubtedly reflect the availability of the male to the married woman, as well as the social stigmas placed on the unwed gravida.

In an analysis of age and parity groups with no reference to marital status (Fig. 2), primiparas show the longer average number of days in both the 15 to 19 and 20 to 29 year age brackets; but do not appear at all in the 30 to 39 year category. A combined average of parities in each of the three age groups shows women at the height of their childbearing years to be more inclined to abstinence, contrary to what one might expect.

For this study, the various complications of pregnancy, delivery, and the puerperium have been considered with no indication as to the degrees of severity, although they ranged from potential to real, and minor to major, difficulties. I have, however, appraised the complications as related or unrelated to coitus. Those deemed probably related to intercourse were puerperal morbidity, false labor, late antepartum bleeding, foul lochia and fever, premature rupture of the membranes, and premature labor. Primary uterine inertia, pre-eclampsia, essential hypertension, cholecystitis, breech presentation, occiput posterior position, and excessive weight gain were examples of complications considered unconnected with coitus, for obvious reasons in each instance.

Puerperal morbidity and foul lochia and fever (Tables II and III) are reviewed together because of their similarity except as to the degree of temperature elevation. One patient having puerperal morbidity and one having foul lochia and fever reported intercourse occurring the last time 7 days prior to admission. Coitus might have been the etiological factor in these cases, but many other factors would need be considered first. The 3 cases of morbidity in the puerperium had an average time coitus of 40 days. None of these were unusual instances of length of labor, duration of ruptured membranes prior to delivery, or method of delivery. The average total blood loss in the second and third stages of labor was 108 ml., and the average duration of the third stage of labor was slightly more than 4 minutes.

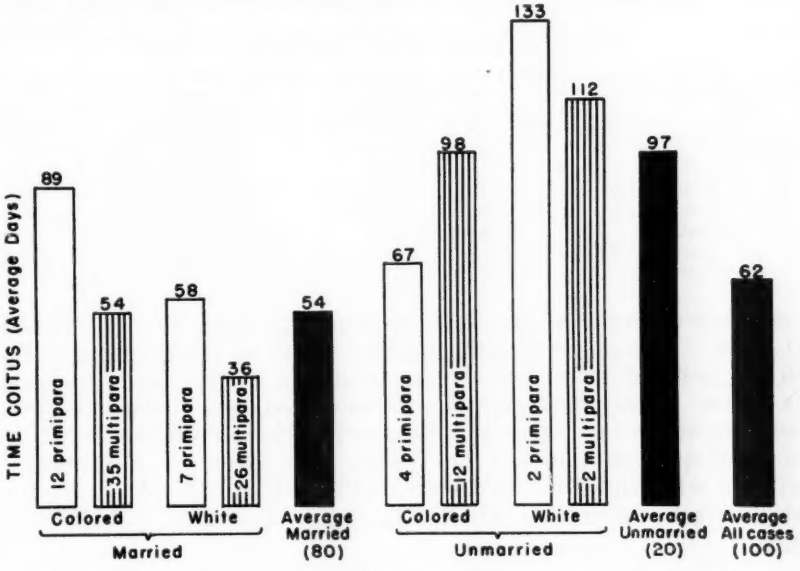


Fig. 1.—Time coitus in relation to marital status, race, and parity.

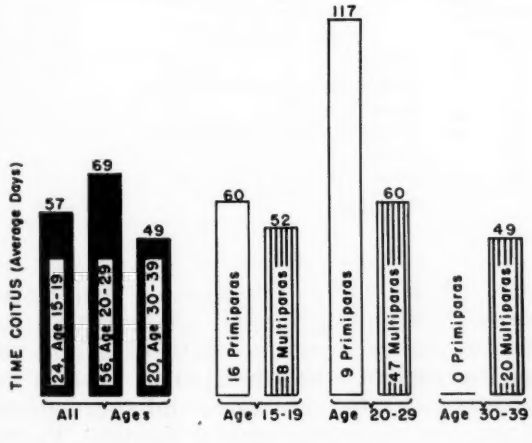


Fig. 2.

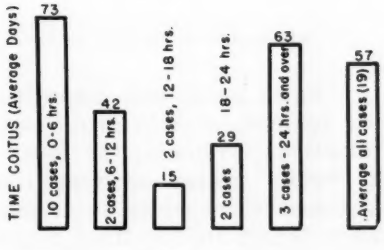


Fig. 3.

Fig. 2.—Time coitus in relation to age and parity.
Fig. 3.—Time coitus in relation to premature rupture of membranes (time prior to delivery).

Neither were any of the 5 cases exhibiting foul lochia and fever unusual, except for one patient, the duration of whose labor was 22 hours and 30 minutes.

In this group of patients, the average total blood loss in the second and third stages was 170 ml., and the duration of the third stage of labor was 6 minutes. The average time of intercourse prior to admission was 49 days.

TABLE II. PUERPERAL MORBIDITY, 3 CASES

TOTAL LENGTH LABOR	DURATION OF RUPTURED MEMBRANES	TYPE DELIVERY	TIME COITUS
6 hrs. 15 min.	45 min.	Spontaneous	7
15 hrs. 35 min.	8 min.	Low forceps	28
14 hrs. 15 min.	5 hrs.	Spontaneous	84
		Average	40

TABLE III. FOUL LOCHIA AND FEVER, 5 CASES

TOTAL LENGTH LABOR	DURATION RUPTURED MEMBRANES	TYPE DELIVERY	TIME COITUS
22 hrs. 30 min.	30 min.	Spontaneous	84
3 hrs. 47 min.	7 min.	Spontaneous	84
1 hr. 32 min.	2 min.	Spontaneous	7
14 hrs.	1 hr.	Low forceps	28
7 hrs. 13 min.	7 hrs. 43 min.	Low forceps	42
		Average	49

Premature rupture of the fetal membranes (Fig. 3) occurred 19 times in the 100 cases. Demonstration of amniotic fluid on sterile vaginal examination prior to the onset of labor was the governing factor in these diagnoses. The 10 patients whose membranes ruptured 0 to 6 hours prior to the onset of labor show the longest average time of intercourse prior to admission. None of these patients developed amnionitis, foul lochia and fever, or puerperal morbidity. Two patients with times coitus 14 and 168 days did, however, have premature labor at 28 weeks' gestation which could not reasonably be attributed to late intercourse.

TABLE IV. FALSE LABOR, 6 CASES

AGE	RACE	PARITY	GESTATION (WEEKS)	ANTEPARTUM COMPLICATIONS	TIME COITUS
18	Negro	0	38	None	140
*18	White	0	37	Antepartum, death of fetus	1
27	Negro	vii	39	Pre-eclampsia	28
22	White	iv	30	Cystitis, stress incontinence	4
28	Negro	v	39	None	42
37	White	v	39	Breech presentation	28
				Average	41

*Spermatozoa present in wet preparation.

False labor was diagnosed 6 times (Table IV). The average time coitus for patients of this group was 41 days. Various incidental antepartum complications occurred, the most serious was the antepartum death of a fetus at 37 weeks' gestation, recognized when the patient was admitted in false labor. The mother reported intercourse 24 hours prior to admission; and spermatozoa were found in the fluid aspirated from the posterior vaginal fornix. Forty-eight hours later the patient was admitted in normal labor. Autopsy failed to reveal the cause of fetal death, but the clinical impression was that an excessively short umbilical cord (20 cm.) was responsible.

Table V is an analysis of the 6 cases in which late antepartum bleeding occurred. Bleeding begun 4 to 6 hours or more prior to the onset of labor was adjudged not incidental to the onset of labor. The average time coitus for all

patients with late antepartum bleeding was 47 days. Vaginal spotting occurred 24 hours prior to the onset of labor in a patient at term who gave a history of intercourse 2 days before admission; spermatozoa were found in the wet preparation in this case. Aside from the spotting, this patient's labor and delivery were uncomplicated. Another patient with a history of coitus 2 days prior to admission had vaginal spotting 18 to 24 hours before the onset of labor, and ruptured membranes 23 hours before delivery; but presented no complications of delivery or the puerperium. While there is at least a possibility that vaginal bleeding may be caused by cervical trauma due to coitus in late pregnancy, figures here do not bear out this theory.

TABLE V. LATE ANTEPARTUM BLEEDING, 6 CASES

AGE (YEARS)	RACE	PARITY	GESTATION (WEEKS)	AMOUNT BLEEDING	TIME PRIOR TO ONSET OF LABOR	OTHER COMPLICATIONS	TIME COITUS
17	Negro	0	40	Spotting	6-8 hrs.	None	56
30	White	iii	40	Spotting	24 hrs.	Excessive weight gain	84
*27	White	v	40	Spotting	24 hrs.	None	2
31	White	ii	40	Spotting	4-6 hrs.	Fever and foul lochia	112
36	Negro	i	38	Spotting	18-24 hrs.	Premature rupture of membranes	2
†24	White	ii	31	Moderate	At time of labor	Premature labor	28
						Average	47

*Spermatozoa present in wet preparation.
†Mild premature separation of placenta.

TABLE VI. PREMATURE LABOR, 9 CASES

AGE (YEARS)	RACE	PARITY	GESTATION (WEEKS)	OTHER COMPLICATIONS	TIME COITUS
*†18	White	0	37	Antepartum death of fetus	1
24	Negro	0	36	None	224
16	White	i	36	None	21
†26	White	iii	33	Pyelonephritis, antepartum death of fetus	28
24	White	ii	31	Premature separation of placenta	28
22	White	iv	30	Cystitis, stress incontinence	4
28	White	v	28	Premature rupture of membranes	14
20	Negro	i	28	Puerperal morbidity	28
25	Negro	iii	28	Premature rupture of membranes	168
				Average	57

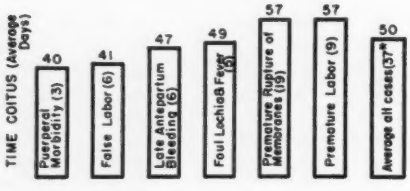
*Spermatozoa present in wet preparation.
†Cause of fetal death unknown.

TABLE VII. COMPLICATIONS UNRELATED TO COITUS, 19 CASES

ANTEPARTUM	INTRAPARTUM	DELIVERY	PUERPERAL	TIME COITUS
12	12	9	7	81 (ave.)

Premature labor complicated pregnancy in 9 of the 100 cases (Table VI). Average time coitus in this classification was 57 days. Included again here is the case of antepartum fetal death discussed under false labor; that of the 18-

year-old white primipara in whose wet preparation spermatozoa were found. In the other antepartum death of a fetus of 33 weeks' gestation, autopsy was not allowed and cause of death is unknown. Neither maternal pyelonephritis nor the fact of a 28 days' time coitus would seem to have an etiological connection with the death. Premature rupture of the membranes occurred 3 and 4 days before delivery, in two patients having premature labor. Time coitus was 168 days and 14 days, respectively. The patient whose puerperal morbidity occurred subsequent to delivery at 28 weeks' gestation reported last coitus 28 days prior to delivery. Again, in these data, there is no evidence to uphold us in our warnings against coitus in late pregnancy.



*Eleven cases had two complications.

Fig. 4.

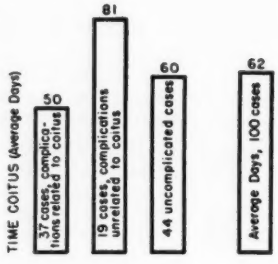


Fig. 5.

Fig. 4.—Various complications related to coitus.
Fig. 5.—Evaluation of entire series.

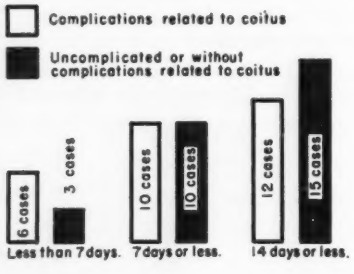


Fig. 6.—Last coitus 14 days or less prior to admission.

Table VII breaks down the complications, thought unrelated to coitus, occurring in 19 cases. Average time coitus for these patients was 81 days. The unusually high number of complications in each category charted in Table VII can be explained by the fact that certain complications, i.e., pre-eclamsia, anemia, and essential hypertension, remained present through the late antepartum, intrapartum, delivery, and puerperal phases of pregnancy, and are recorded under each phase.

Analysis of Results

Thirty-seven of the 100 patients that comprise this series exhibited 48 complications in the late antepartum and puerperal period (11 patients had 2 complications). All of the types of the 48 complications encountered could conceivably have been a result of coitus, but the average time coitus for these complications (Fig. 4) is sufficiently long that coitus seems improbable as the etiological factor. Also, there is no evidence to hold coitus responsible for the various complications in specific cases where recent coitus is cited.

An evaluation of the entire series (Fig. 5) in relation to the average times of last intercourse prior to admission, reveals that complications adjudged re-

lated to intercourse have an average time coitus of 50 days. This average time is shorter than that for the complications unrelated to coitus; and shorter than that for the uncomplicated cases; and shorter than that for all the cases. However, these averages have no statistical significance.

Twenty-seven patients of the 100 interviewed stated that their last coitus occurred 14 days or less prior to admission (Fig. 6). Twelve of this group had complications that were possibly related to coitus; while 15 cases were uncomplicated, or without complications related to coitus. In the group of those having their last coitus 7 days or less prior to admission there were 10 cases in each category. And in that group reporting time coitus less than 7 days, there were 6 with complications possibly related to coitus; and 3 cases uncomplicated, or without complications related to coitus. Of the 6 cases with complications possibly related to coitus, 2 were false labor; 2 were late antepartum spotting, 18 to 24 hours prior to the onset of labor; two were premature labor—1 case (previously discussed) of a 37 weeks' gestation with antepartum death of the fetus; and one case at 30 weeks' gestation with no other complications.

Summary and Conclusions

One hundred cases are surveyed as to the effects of coitus on late pregnancy, delivery, and the puerperium. For the purpose of appraisal, cases have been classified as those with complications related to coitus and those with complications unrelated; and uncomplicated cases.

Conclusions must necessarily rest on further investigation. I hope that the results of this present study will stimulate that investigation, and will encourage us to de-emphasize abstinence during the final weeks of pregnancy, since time coitus appears to be of little significance, provided that the gravida is not uncomfortable during intercourse.

I wish to thank Dr. Frank L. Fernandez, Dr. Meyer J. Fleischman, and Dr. Barton T. Smith for their aid in collection of the data.

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VARIATION IN SIZE AND WEIGHT OF TWINS OF MONOCHORIAL PREGNANCIES

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THAT twins may differ in size is a well-recognized fact. According to Eastman,[1] "It is not unusual in twins to differ considerably in size and weight, especially when derived from a single ovum." Ahlfeld has reported cases in which living twins weighed, respectively, 2,320 grams, 1,120 grams, 1,920 grams and 790 grams. Greenhill[2] states, "Twins usually differ in weight and length from each other and sometimes the differences are considerable." Beck,[3] as well, asserts that "twins usually are smaller than other infants and occasionally one weighs considerably less than the other." None of these authors suggests any explanation of this phenomenon. Neither can any be found in current literature. It is the purpose of this report to offer a possible etiology of the variation in the size of twins, in at least some cases.

The report is based upon the observation of four cases of twins. In one case, one of the twins was blighted. In the other three, there was a marked difference in size and weight of the twins in each instance. The one striking feature in each of these cases was the abnormal insertion of the cord of the smaller, less developed twin. In the first case, the cord of the blighted fetus had a velamentous insertion. In the remaining three, the cord of the smaller fetus was inserted marginally in each placenta. The cord of the corresponding fetus was recognized in each case by clamping the placental end of the severed cord of the first infant with one clamp and of the second with two.

A brief description of the cases follows:

CASE 1.—A. G., a 28-year-old white woman, was admitted to the hospital on Aug. 4, 1950, in active labor. Her expected date of delivery was Sept. 9, 1950. Her prenatal course was entirely uneventful. At the end of four hours and forty minutes of labor she delivered, spontaneously, a female infant weighing 2,300 grams (5 pounds, 1 ounce). The baby appeared normal and had a prompt cry. The placenta was delivered ten minutes later. Upon examination, the cord was found to arise eccentrically near the margin. About 20 cm. from the opposite margin of the placenta there was another cord inserted in the membranes. Attached to the other end of this cord was a blighted fetus. It was well preserved, not macerated, 5 cm. long, and, judging by its appearance, must have died at the age of 8 to 10 weeks (Figs. 1 and 2).

This, then, was a monochorial twin pregnancy with one twin blighted, due to the velamentous insertion of the cord. The circulation of the latter was apparently interfered with, due to the anomalous insertions, causing the death of the fetus during the first trimester with subsequent flattening as a result of pressure exerted upon it by the surviving fetus. That this is not uncommon in cases of blighted fetuses was brought out by Kindred,[4] who, in an exhaustive study of this subject, showed that, in 21 cases of monochorial twin pregnancies

with one twin blighted due to anomalies of the cord, there were 5 cases of velamentous insertion of the cord, while, in a corresponding group of dichorial pregnancies, there was only one case of velamentous insertion of the cord.

CASE 2.—I. B., a 36-year-old white woman, was admitted to the hospital at 6 A.M. on Sept. 16, 1950, complaining of mild labor pains. Her expected date of delivery was Nov. 11, 1950. The antenatal course was uneventful except for an excessive enlargement of the uterus.

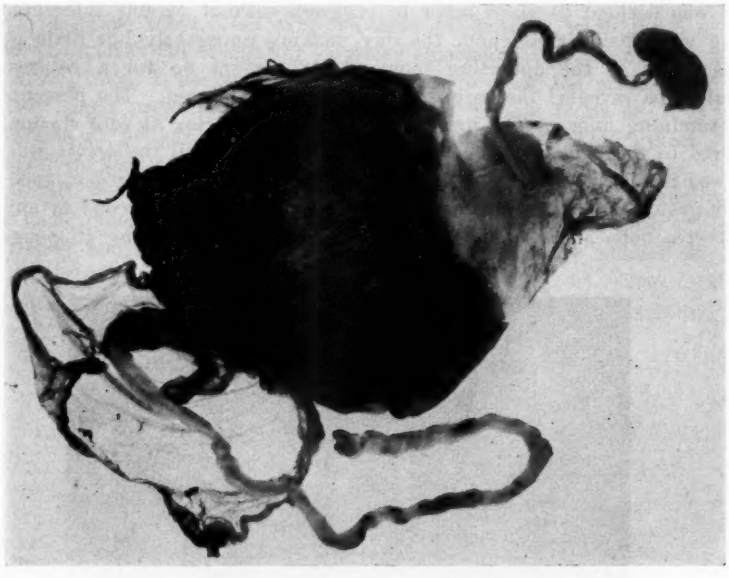

Fig. 1.—Placenta of Case 1 with cord of living infant arising at margin while the cord of the blighted fetus has a velamentous insertion.

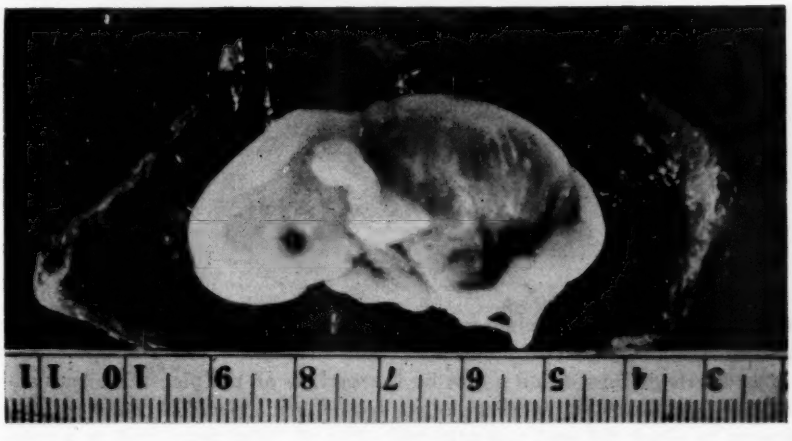

Fig. 2.—Close-up view of blighted fetus.

A roentgenographic examination a few weeks prior to admission showed the presence of twins. The general condition of the patient upon admission was good. Her blood pressure was 108/60; her pulse was 74 per minute and of good quality. The uterus was high and very distended. One fetal heart was distinctly audible over the left lower quadrant. No other fetal heart could be heard. The patient was having mild irregular pains every 5 to 8 minutes. About one hour after admission the membranes ruptured. There was an escape of a large amount of amniotic fluid, deeply blood tinged, as well as some blood clots. The patient went

into shock. Her pulse became feeble and her blood pressure could not be obtained. An intravenous injection of 5 per cent glucose in saline was immediately started followed by a blood transfusion fifteen minutes later. The patient responded promptly. The quality of her pulse improved and the blood pressure rose gradually, and at 9 A.M. it registered 120/80. The fetal heartbeat was still heard over the left lower quadrant and was of good quality. There was no vaginal bleeding and the patient began to have pains every 7 to 8 minutes. A provisional diagnosis of marginal placenta previa was made. Since the patient's condition was favorable, it was decided to allow labor to progress without outside interference. She continued having weak pains throughout the day, making apparently but little progress. At 7 P.M. she was taken to the operating room which was set up for a cesarean section. A vaginal examination revealed the cervix to be 6 to 7 cm. dilated. The placenta could not be felt by the examining finger. The presenting part was a vertex at zero station. The patient was transferred to the delivery room and allowed to labor until the cervix was fully dilated. A baby boy was then delivered by low forceps application. He appeared in good condition and weighed 2,000 grams (4 pounds, 6 ounces). Five minutes later the second infant was delivered by outlet forceps, pale, stillborn, not macerated, weight 1,020 grams (2 pounds, 4 ounces).

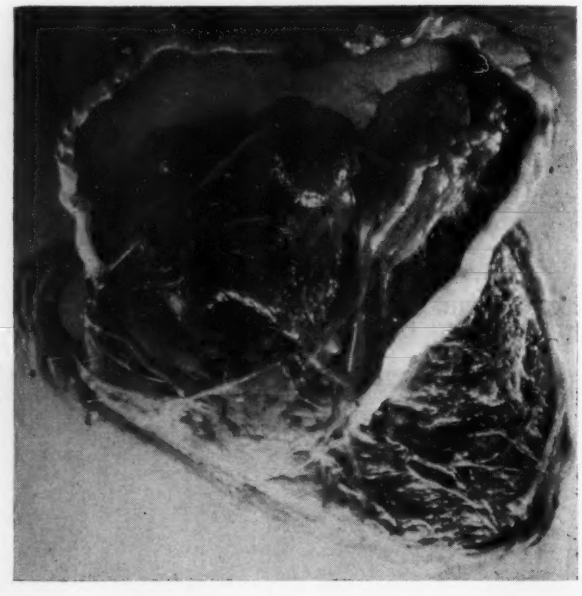

Fig. 3.—Placenta of Case 2 showing marginal insertion of cord of smaller stillborn infant with hemorrhage into cord.

The placenta was delivered five minutes later. It was monochorial with a clot at the margin where the cord of the second baby was attached. The cord had a marginal insertion with evidence of hemorrhage into it and a clot on the surface of the placenta adjacent to the cord. This, then, was a case, not of placenta previa, but of hemorrhage in the cord and the margin of the placenta to which the cord was attached (Fig. 3). The fetus died as a result of hemorrhage into the cord. Of special interest was the fact that the smaller, less developed fetus had a marginally inserted cord. The significance of this will be discussed later.

CASE 3.—R. R., a 35-year-old white female, was admitted to the hospital on May 9, 1951, with a history of profuse vaginal bleeding. Her expected date of delivery was June 15, 1951. The patient had an episode of vaginal bleeding three weeks prior to admission, at which time she remained in bed until the bleeding stopped. On the night of admission she had a profuse, painless attack of vaginal bleeding and she was ordered to the hospital immediately. Her general condition was good. The blood pressure was 118/84. The fetal heart-

beat was heard over the right lower quadrant and was of good quality. The vaginal bleeding persisted. A diagnosis of placenta previa was made and a classical cesarean section was performed. Two female infants were delivered, weighing 2,000 and 1,100 grams (4 pounds, 7 ounces, and 2 pounds, 7 ounces), respectively. The placenta was situated in the lower segment of the uterine cavity completely covering the cervical os. It was monochorial and the cord of the smaller baby was marginally inserted (Fig. 4).

CASE 4.—E. D., a 24-year-old primigravida, was admitted to the hospital on March 11, 1952, at 4 A.M., in active labor. Her expected date of delivery was March 4, 1952. The antenatal course was uneventful except for excessive enlargement of the uterus. A roentgenographic examination, taken 2 weeks prior to admission, revealed the presence of twins. The patient made very rapid progress and was delivered of female twins at 10 A.M. Baby A weighed 3,430 grams (7 pounds, 9 ounces) and Baby B weighed 1,445 grams (3 pounds, 3 ounces). The amniotic fluid of the sac of Baby B was deeply meconium stained. The placenta was monochorial. It was 30 cm. long and 18 cm. wide, divided into unequal parts by the fused amniotic membrane. In the larger portion, 18 cm. long, the cord of Baby A was inserted eccentrically about 5 cm. away from the margin. In the smaller portion, 12 cm. long, the cord of Baby B was inserted at the very margin (Fig. 5). The fetal surface of the smaller portion was meconium tinged. The maternal side was congested and deeply cyanotic. Baby B was transferred to a premature center and did well.

Fig. 4.—Placenta in Case 3 showing marginal insertion of cord of smaller fetus.

Comment

According to Eastman,[5] "The umbilical cord is usually inserted eccentrically upon the fetal surface of the placenta somewhere between the center and the periphery. A central insertion is less common while in a still smaller number of cases the junction has taken place near the margin. These variations possess no clinical significance." Greenhill[6] likewise states "battledore placenta (marginal insertion of the cord) has no clinical importance." That there are exceptions to these assertions has been recently shown by Donnelly,[7] who reported eight cases of battledore placentas and one of circumvallate in which some degree of bleeding occurred during pregnancy or labor in each case, and which

were often mistakenly diagnosed as placenta previa. Cesarean sections were performed in two of these cases. Case 2 reported here illustrates the same point. There was a marked hemorrhage during labor which proved to originate from the region of a marginally inserted cord. In this instance there was sufficient damage to the cord to cause intrauterine death of the fetus.

As stated previously, velamentous insertion of the cord occurs more frequently in twins than in single pregnancies and more frequently in monochorial than in the dichorial variety. Von Franqué's explanation of the origin of this anomaly is universally accepted today. Torrey[8] explained von Franqué's theory as follows: "The abdominal pedicle ordinarily extends to the fetus from that portion of the chorion which is in contact with the most richly vascularized portion of the decidua. Usually this is the decidua basalis. In this way the cord becomes inserted upon the placenta. However, occasionally, during the first few days of pregnancy, the area of greatest vascularization may be in the capsular portion of the decidua and, in such circumstances, the abdominal pedicle takes its origin from that location. As the pregnancy progresses, however, the

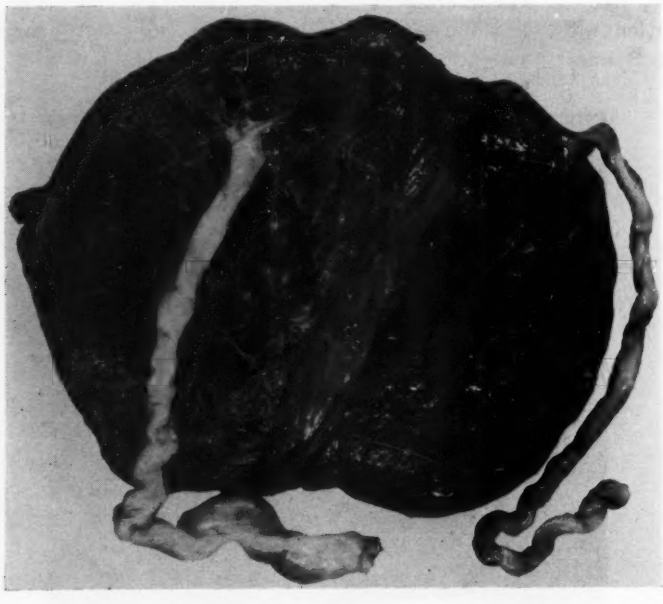

Fig. 5.—Placenta of Case 4. Note insertion of cord at extreme margin and the difference in size between the two portions of the placenta.

area of vascularization shifts to the basalis portion of the decidua (the actual site of the future placenta) while the abdominal pedicle retains its original position and, from its maternal end, the vessels extend to the margin of the placenta." It is evident from this explanation why the frequency of velamentous insertion of the cord is greater in twins, especially in the monochorial variety. In the presence of two fetuses instead of one, the chance that the pedicle of one of them will extend from the capsular portion of the decidua rather than from the basalis is twice as great. Carrying this thought further, it is quite conceivable that the same principle may apply to marginal insertion of the cord. While there are no statistical data available, it would appear, from general observation, that marginal insertion of the cord is not infrequent in twins. A study of this subject is in progress at the present time.

Marginal insertion of the cord may have some clinical significance in that it may affect the development of the fetus, especially in the last trimester.

Reynolds[9] states that the growth and maturation of the fetus after conversion of the uterus depends, to an important degree, upon the conditions of circulation of maternal and fetal bloods, respectively, through the organ of exchange, the placenta. Thus, a proper uterine environment of the fetus must be considered in any rounded discussion of fetal growth, since this does not depend upon genetic forces within the fetus alone. He further states that the pressure at term on the placental vascular bed reduces the amount of nutriment available to the fetus, thus modifying its further growth.

In multiple pregnancy, the uterus is greatly distended in the last trimester, resulting in an ever-increasing intrauterine pressure. The thinned-out peripheral portion of the placenta is compressed more easily than its thicker central portion. If one of the cords is inserted at or near the margin, it is conceivable that the vessels of this cord, as well as the adjacent portion of the placenta, may become compressed, to a degree sufficient to interfere with the adequate blood supply of the corresponding fetus and thus slow up its further development and growth. This possibility has been substantiated by Potter[10] who, in discussing infant mortality in twin pregnancies, states, "If one cord is attached peripherally and is supplied by only one portion of the placenta, the inadequate size of the capillary bed may be responsible for malformation or fetal death." In less extreme cases of circulatory interference, the result may not be malformation or death of the fetus but only a slowing of its growth.

This hypothesis is illustrated in the cases cited in this report. In the first case, because of a velamentous insertion of the cord, the circulation was shut off completely at an early stage of pregnancy, causing the death of the fetus. In the other three cases, in which there was a marginal insertion of the cord in monochorial twin pregnancies, the circulation was diminished to a degree sufficient to interfere with the growth of the corresponding fetus. This was borne out most strikingly in Case 4. There were no complications here such as placenta previa or hemorrhage into and around the cord as in the two other cases reported. The placenta with the marginally inserted cord was definitely smaller and appeared congested and cyanotic. The fetus was in distress, as evidenced by the meconium-stained amniotic fluid, and weighed 1,985 grams (4 pounds, 6 ounces) less than her sister. It thus may appear that the variation in size of twins, particularly in the monochorial variety, may, in some instances at least, be caused by the fact that one of the cords is inserted in the margin of the placenta. The blood supply of the corresponding fetus may then become diminished, resulting in interference with development and growth.

Summary

1. Four cases of monochorial twin pregnancies are presented with anomalous insertion of one of the cords in each case. The complications associated with these anomalies are pointed out.

2. In one case there was a velamentous insertion of one of the cords with the twin blighted during the first trimester of pregnancy.

3. In the other three, each had a marginal insertion of one of the cords. In one instance, there was a hemorrhage in the cord and the adjacent part of the placenta, with subsequent intrauterine death of the fetus. In another, there was evidence of fetal distress. In all three cases, the fetus of the marginally attached cord was considerably smaller than its twin. In Case 4, the difference in weight was 1,985 grams.

4. A reason for the incidence of marginal insertion of the cord in twins, especially in the monochorial type, is suggested.

5. A possible explanation of the variety in the weight and size of twins is offered.

The author wishes to thank Dr. S. F. Scuderi and Dr. L. P. Seitsive for permission to use their cases for this report.

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ARTERIECTASIA OF THE UTERINE ARTERY

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IN 1926, Dubreuil and Loubat[1] reported a case "probablement sans précédent," under the title "Aneurysme circoide de l'uterus," in which they brought to medical attention the first published case of the so-called "cirsoid aneurysm" of the uterus. Since that time two additional cases have been reported.[2, 3] A review of the literature together with a fourth similar case is now presented because of its rarity, the unusual clinical picture, and because of the interesting considerations which were unearthed in attempting to sharply define and describe the pathologic findings.

Review of the Literature

An extensive review of the literature was made in an attempt to find cases similar to the one to be described. The search was complicated by the possibility that descriptions of this vascular tumor might have been hidden under other designations in the literature. Careful searching through the Index Catalogue of the Library of the Surgeon General's Office of the United States Army, the *Quarterly Cumulative Index Medicus,* the Academy of Medicine Card Catalogue File, and the *Index Medicus* (from 1880) revealed only three comparable case reports in which an abnormality of the uterine blood supply (within the uterus) was presented. Innumerable cases of dilatation and/or aneurysm of the uterine artery, occurring outside the uterus, were found, and are not included in this review.

The first reported case having facets similar to the present case report was presented by Dubreuil and Loubat[1] in 1926. The authors gave an "anatomical-pathological" study in which a 62-year-old woman, gravida iv, para iv, nine years postmenopausal, was seen for irregular vaginal bleeding. Pulsating vessels were felt in both fornices. A diagnosis of "telangiectatic tumor" of the uterus was made and a hysterectomy was contemplated. At the operating table, the uterus was found to be enlarged, erectile, and vibration of the uterus could be seen and felt. A subtotal hysterectomy was done with difficulty because of stump bleeding. The patient died postoperatively of intestinal obstruction and peritonitis after subsequent cecostomy.

The authors included photomicrographs, and described the uterus as grossly enlarged, microscopically showing a scattered intertwining network of vessels throughout the muscular wall. These vessels varied from 1 mm. to 2 cm. in diameter. It could not be determined whether they were arteries or veins. An internal elastic lamella was present, although often distorted; the intima was frequently thickened and showed smooth muscle fibers and connective tissue; an external elastic lamella was variably present or absent. The findings were described as a cirsoid aneurysm similar to the type seen in more superficial parts of the body.

The second case was presented by Graves and Smith[2] in 1927. A 62-year-old gravida v, para iv, was seen because of postmenopausal bleeding (menopause at 48). On examination, the uterus was thought to be enlarged and pulsations were felt. A diagnosis of carcinoma of the fundus was made. Curettage resulted in profuse hemorrhage. Packing and laparotomy followed. At operation, an enlarged, engorged, spongy, pulsating uterus was found. This patient had a postoperative hemiplegia. The specimen in this case showed large and small blood vessels with walls of varying thicknesses, in which intima, media, and adventitia could not be clearly distinguished in many areas. "To distinguish arteries from veins was impossible except in rare instances where the elastic tissue was so characteristically arranged as to leave no doubt about the arterial character of the vessel."

The third case was reported by Reynolds, Owen, and Cantor[3] in 1949. A white, 42-year-old woman was admitted for severe headaches at the time of her menstrual periods, with the finding of a soft enlarged uterus. Diagnostic curettage was attempted. As soon as the Hegar dilator was inserted into the cervical canal, tremendous hemorrhage occurred. The uterus was packed, Pitocin was administered intramuscularly, and a supracervical hysterectomy was performed. The vessels in both broad ligaments and on the uterus were tortuous and large. A second operation was necessary because the patient went into postoperative shock as a result of a bleeding vessel in the pelvis. After the second operation and complete hemostasis, this patient made an uneventful recovery. The uterus measured 6 by 6 by 5 cm., the serosa was smooth, there were cystic spaces in the myometrium with fibrosis of the myometrium and hypertrophy of the muscular walls surrounding the blood spaces. It was impossible to demonstrate any connection between artery and vein.

In the three cases cited above, it proved impossible to differentiate definitely segments of vessels as artery or vein. The case of Dubreuil differs strikingly in that the pathologic vessels were distributed throughout the uterine wall, while in the other two cases, the areas of intertwining vessels were more sharply localized. In these cases, no mention of a successful dissection is made, and therefore a description of the dissected vessels was not possible.

Case Report

N. C., No. 1892-51, a 63-year-old Puerto Rican woman, was admitted on Feb. 17, 1951, because of postmenopausal vaginal bleeding associated with low back pain of seven days' duration.

The patient had had an uneventful menopause eight years before, and apparently had been asymptomatic until one week prior to admission, when she noted the onset of vaginal bleeding which was not associated with pain. Four days before the present admission, the patient had been hospitalized at another hospital and had required vaginal packing because of profuse bleeding. After 12 hours, the packing was removed and a curettage was attempted.

Under anesthesia, the vagina admitted two fingers, the uterus was slightly enlarged. No adnexal masses or other abnormalities were detected. Hegar dilators were inserted into the cervix; this was followed by no significant bleeding. A small curette was then used. When the left half of the uterine fundus was curetted, only small clots and slight bleeding resulted. However, when the right half of the fundus was curetted, bright red blood appeared in a profuse outpouring. Approximately 200 c.c. of blood were lost in a few seconds, and intrauterine and intravaginal packing was inserted. Ergotrate was given intravenously. No drop in blood pressure was noted; the bleeding apparently had been controlled by these measures. No tissue was obtained. When the packing was removed

on the following day, minimal bleeding occurred. For economic reasons, the patient signed herself out of the hospital and was admitted to Morrisania City Hospital two days later with moderate vaginal bleeding and low back pain.

The patient was a gravida x, para viii, with 5 living children. Further obstetrical history was not obtainable, the patient apparently having had all normal spontaneous deliveries in Puerto Rico. Menses prior to the menopause had been normal starting at 13 years of age, every 28 days for 5 days with slight dysmenorrhea. Medical, surgical, and venereal history were noncontributory.

Examination showed the patient to be in no acute distress, asymptomatic except for moderate painless vaginal bleeding. Examination of head and neck, chest and heart yielded no significant findings. No petechiae nor other external manifestations of vascular disease were present. The abdomen was obese and soft; no masses nor tenderness were found. On pelvic examination, the introitus was parous; there was moderate bleeding; the cervix was anterior and slightly irregular; the uterus was enlarged to six weeks' gestational size. No adnexal masses were palpated. Speculum examination revealed a small cervix and an atrophied vaginal vault. No pulsations were noted in the course of pelvic examinations. The temperature was 101° F.; pulse and respiration rates were normal. The blood pressure was 100/70. The sedimentation rate was 24 mm. in 30 minutes (Westergren). Hemoglobin was 12 Gm. Urine and Wassermann test were negative. Blood urea nitrogen was 14 mg. per cent; fasting blood sugar was 85 mg. per cent. Chest x-ray showed a slightly elongated aorta.

Because of the history of recent interference, the elevated sedimentation rate, and elevated temperature, the possibility of a perforation of the uterus was considered. It was felt that the most likely diagnosis, however, was a fundal malignancy. After three days of treatment with procaine penicillin and bed rest, the temperature returned to normal. During this time, short sporadic periods of brisk bleeding occurred. A Papanicolaou smear was reported as showing "several suspicious cells."

Because of persistent vaginal bleeding, a laparotomy under gas-oxygen-ether anesthesia was performed on Feb. 27, 1951. The peritoneal cavity was easily entered; no adhesions were found. The uterus was found to be anterior, enlarged to eight weeks' size, soft, smooth, and lobular, with several irregular areas on the right posterior fundus. Because it was felt that the uterus was the site of a malignancy, and in order not to spill the contents of the uterus in the peritoneal cavity, no perforating instruments were used on the uterus for traction. A total hysterectomy and bilateral salpingo-oophorectomy were done. The vessels of the right broad ligament were noted to be tortuous and very prominent. When the right uterine artery was clamped and cut, its lumen was noted to be approximately ⅜ of an inch in diameter. Considerable difficulty was encountered in the region of the right cardinal ligament because of persistent bleeding from many apparently engorged vessels. All bleeding was finally controlled, and peritonization of the vaginal vault and stumps was performed without incident. Because of thin, friable parietal peritoneum, the abdomen was closed with through-and-through silk sutures and interrupted chromic catgut sutures.

The patient received a 1,000 c.c. blood transfusion and was returned to the ward in good condition. The postoperative course was uneventful, the silk through-and-through sutures were removed on the fourteenth day, and the patient was discharged in good condition on the twentieth postoperative day.

Gross Pathology.—

Examination of the gross specimen revealed a uterus measuring 15 by 10 by 10 cm. It was soft, hyperemic, and slightly globular at the fundus. The posterior surface of the right half of the uterine fundus was irregular and bulging. The cervix was stenotic. The right uterine artery was noted to be tortuous and dilated; the left was of normal appearance. None of the major veins appeared to be dilated. The tubes and ovaries appeared atrophic.

On opening the uterus by a longitudinal incision, about 60 c.c. of blood clot in the form of a cast of the endometrial cavity were found. Projecting into the endometrial

cavity from the right fornix was a soft cystic mass 5 cm. in diameter. The overlying endometrium, which was displaced downward by the mass, appeared grossly intact.

After incision of the thin layer of overlying endometrium, a cluster of variable-sized convoluted vessels could be seen, the largest of which was 0.5 cm. in diameter (Figs. 1 and 2). Upon injection of the right uterine artery, dye appeared in the labyrinth of vessels; injection of the left uterine artery revealed no continuity with the pathologic area.

Fig. 1.—Gross specimen of the uterus, tubes, and ovaries, with uterus opened longitudinally, revealing a dilated vessel mass at the fundus incised to show cross section.

Fig. 2.—Close-up view of gross specimen revealing "cirsoid" effect at fundus.

The vessel mass was bound together in a serpentine helical fashion by strands of connective tissue. The largest component vessel, when dissected, was seen to be a single dilated vessel continuous with the dilated right uterine artery and breaking up into tiny vessels which coursed into the myometrium. The entire cystic mass was localized to the fundus and bulged into the endometrial cavity.

Microscopic Pathology.—Multiple microscopic sections were taken along the course of the dilated vessels. The vessels that were sectioned varied in size from 1 to 5 mm.

The intima varied from a thin to a markedly thick layer with frequent abrupt transitions between the two. The internal elastic lamella was present, but was often reduplicated and frayed (Fig. 3).

Fig. 3.—Section of vessel showing intimal thickening, reduplication, and fraying of the internal elastic lamella. (× 100.)

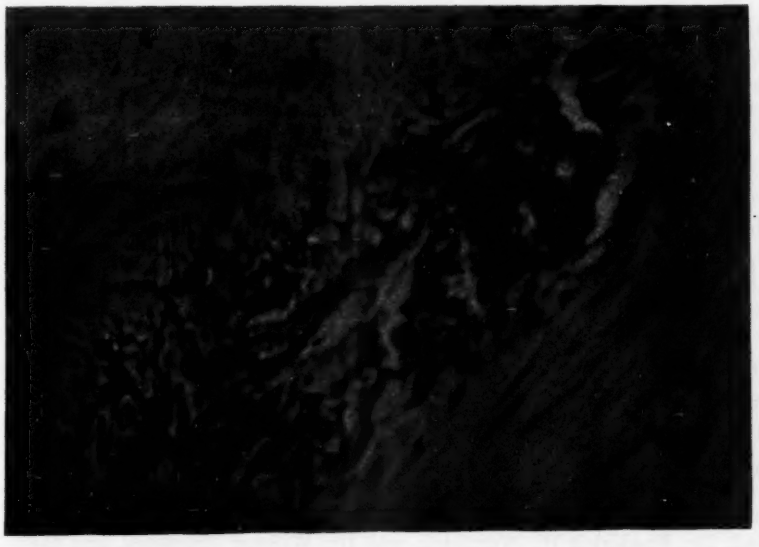

Fig. 4.—High-power view of media showing areas of calcification. (× 440.)

The media varied from a broad wall with well-preserved smooth muscle fibers to areas where there was marked fibrous tissue proliferation, with thickening of the wall, and diminished numbers of smooth muscle fibers. Focal areas of calcification were noted in some of the thickened portions of the vessel walls (Fig. 4). Vasa vasorum were well preserved and showed no exudate.

An external elastic lamella could not be distinguished. The adventitia of the vessels blended imperceptibly with the surrounding connective tissue.

The endometrium was atrophic throughout, with occasional scattered eosinophils, grouped principally about tiny vessels. The myometrium showed considerable fibrosis. Well-defined tiny vessels identifiable as arterioles and venules could be seen lying side by side in the myometrial mass.

Comment

Several interesting pathologic and clinical considerations were encountered in the analysis of this case.

The problem of classification of the specimen was complicated by the lack of universal acceptance in the literature of the criteria for defining cirsoid aneurysm. If we accept Meleney's[4] definition of a cirsoid aneurysm as a "pulsating tumor caused by an anastomosis between small arteries and veins without the interposition of capillaries," our specimen cannot be definitely classified as a cirsoid aneurysm. The finding throughout the dissected portion of the uterus, of vessel walls of essentially uniform structure with an intact internal elastic lamella and a broad muscular media, even in the absence of an external elastic lamella, is consistent with the structure of an artery.[5] Furthermore, the structure was well localized, and, in its greatest portion, could be dissected into a single vessel. Therefore, in strict conformity with the limits of our findings, we prefer to describe our specimen as an "arteriectasia."

In the three cases cited from the literature,[1, 2, 3] and in similarly described entities from other parts of the body,[6, 7] the term "cirsoid aneurysm" was used, although it proved impossible to demonstrate definitely communications between arteries and veins. In contrast, however, in Meleney's case[4] of a cirsoid aneurysm of the jaw, there were "not only definite arteries and definite veins but intermediate forms."

The finding of sclerotic changes in the vessels in our case and that of Reynolds and associates[3] re-emphasizes Reynolds' suggestion that arteriosclerotic changes are a factor in the etiology of the bleeding. The work of Vogelsanger,[8] demonstrating widespread arteriosclerotic changes in the vessels of women over forty, whose uteri were carefully studied at autopsy, further supports this view.

Summary

1. A review of the literature and a case report of a rare condition are presented.

2. Bleeding from vascular tumors of the uterus should be considered in the differential diagnosis of uterine bleeding, especially in the postmenopausal woman.

3. It must be remembered that an attempt to curette will result in a dangerous hemorrhage; the diagnosis of vascular tumor of the uterus must be entertained if unexplained profuse bleeding follows a curettage.

4. At laparotomy, difficulty may arise in controlling bleeding from the stumps due to engorgement of vessels.

The authors gratefully acknowledge the assistance and advice given by Dr. Milton J. Goodfriend, Dr. Frederick W. Wurzbach, and Dr. William Aaronson, and their cooperation.

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OVARIAN PREGNANCY*

Case Report With Discussion of Controversial Issues in the Literature

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THROUGH the years much confusion has arisen concerning various aspects of ovarian pregnancy. The purposes of this paper are: (1) an attempt to clarify these controversial issues by analysis of the reported cases up to March 1, 1951; (2) to present a case of postterm ovarian pregnancy with dead fetus. Ninety cases, including the authors', were reviewed with emphasis upon incidence, diagnostic criteria, classification, and etiology.

Pertinent Facts From Review of Literature

The average age of the women operated upon for ovarian pregnancy was 30 years. Of 71 patients with adequate histories, 35 (49.3 per cent) had had no previous pregnancies and sterility was a common complaint. Multiple spontaneous abortions were frequently found in the same patient prior to ovarian conception. Only 64 (65.9 per cent) of 97 previous pregnancies in the other 36 patients reached a viable stage. The signs and symptoms of ovarian pregnancy were almost synonymous with those of ectopic pregnancy in general. Preoperative diagnosis was ectopic or tubal pregnancy in 54 (60 per cent) of the cases, while in 36 (40 per cent) of the cases the diagnoses included nearly every intrapelvic disease with which women are afflicted.

Of the 90 ovarian pregnancies 68 (75.5 per cent) were terminated by the end of the first trimester. Another 11 (12.2 per cent) terminated in the second trimester and another 11 (12.2 per cent) lasted to the third trimester or beyond. Of the viable gestations 7 infants (63.3 per cent) were stillborn and 4 (36.4 per cent) were alive at birth. Two (18.2 per cent) of the viable babies were grossly malformed.

The postoperative diagnosis was simply "ovarian pregnancy" in 50 (55.5 per cent) cases. Other diagnoses were extrafollicular 2 (2.2 per cent); intrafollicular 13 (14.4 per cent); juxtafollicular 2 (2.2 per cent); primary 14 (15.5 per cent); true 6 (6.6 per cent); superficial 2 (2.2 per cent); cortical 1 (1.1 per cent). Additional diagnoses were chronic salpingitis in 14 (15.5 per cent) and endometriosis in only 2 (2.2 per cent).

Comment on Controversial Issues in the Literature

Incidence.—The number of authentic cases reported in the literature is difficult to evaluate. Including the cases reviewed up to March 1, 1951, and based on Courtiss'[2] report in 1942, the total number of cases is 125. Using Wittenberg and Ries'[11] figures as the basis, the total is only 94 cases to the same date. Presumably up until March 1, 1951, the authentic cases reported number well over 100.

*Read at the monthly meeting of the Rio Grande Valley Obstetrical and Gynecological Society, May 7, 1951.

On the basis of Courtiss'[2] and the Methodist Hospital of Dallas'[5] figures, the average incidence of ectopic to uterine pregnancy is 1 to 209. The average incidence of ovarian to ectopic pregnancy as computed from various sources was 1 to 117. Correlating these figures would give the incidence of ovarian to intrauterine pregnancy as 1 to 24,453.

Criteria.—The basic criteria for diagnosis of true ovarian pregnancy were established in 1878 when Spiegelberg[9] published the four postulates as follows: (1) The tube, including the fimbriated end, must be intact, and must be distinctly separate from the ovary. (2) The gestational sac must definitely occupy the normal position of the ovary. (3) The gestational sac must be connected to the uterus by the uteroovarian ligament. (4) Unquestionable ovarian tissue must be demonstrated in the walls of the sac.

Norris[6] in 1909 further amplified the first postulate by stating that the tube must show no microscopic evidence of pregnancy. Stander[10] enlarged on the fourth postulate by requiring ovarian tissue to be found in several places at some distance from each other in the wall of the sac.

The authors would like to submit a modification primarily of the fourth postulate but also bearing on the first postulate. In several cases reviewed the extraneous tissue was adherent to the gestational sac but ovarian tissue lay between this extraneous tissue and the fetal tissues. That is, ovarian tissue formed an intact covering for the fetal sac with other tissue, usually salpinx, adherent to the ovary yet not coming into direct contact with fetal tissues. These cases should be classified as true ovarian pregnancies. Therefore, further modification of Stander's[10] previous qualification is suggested as follows: Unquestionable ovarian tissue must be demonstrated in the walls of the sac in several places at some distance from each other and intervening *between* fetal tissues and any adherent extraneous tissue. It is felt that this added modification will serve properly to place the individual cases into the ovarian or nonovarian classification more easily and accurately.

Classification or Type.—As noted previously, 55.5 per cent of the 90 cases reviewed were diagnosed simply as "ovarian pregnancy" without regard to specific classification. The other 44.5 per cent had a total of 7 different types of ovarian pregnancy classifications. These facts show the desirability of a basic, fundamental, simplified method of ovarian pregnancy nomenclature. The proposed classification is not necessarily new but is a consolidation and simplification of previous methods. Its purpose is not to form a theoretical, but instead, a practical, functional classification. It is based fundamentally on the site of implantation and later development of the fertilized ovum rather than on the site involved where fertilization first occurred:

1. Primary ovarian pregnancy: Ovarian tissue forms a complete intact layer around the fetus and fetal tissues. In the case of ruptured ovarian pregnancy the site of rupture must have been through a previously intact layer of ovarian tissues. Extraneous adherent organs or tissues will not alter this classification if ovarian tissue lies *between* them and the fetal tissues.

A. Intrafollicular: The fertilized ovum is implanted and develops in the Graafian follicle.

B. Extrafollicular: The fertilized ovum is implanted and develops in ovarian tissue other than in the Graafian follicle. This type would include juxtafollicular, interstitial, cortical, and superficial implantation.

2. Combined ovarian pregnancy: This type of ovarian pregnancy would be that in which ovary formed at least a portion of the tissue lying adjacent to fetal tissues but not forming the entire wall by itself. In addition, forming the rest of the sac wall and lying adjacent to fetal tissues would be other organs

or tissues. An example of this would be tubovarian pregnancy in which both types of tissue were in intimate contact with fetal tissue.

This leaves the classification of ovarian pregnancy, as stated above, as simple and practical as possible, yet even with this classification it will be very difficult to place the individual cases of ovarian pregnancy, particularly those past the third month, in the proper category.

Etiology.—Theories of etiology in the past have been primarily mechanical in nature with the belief that fertilization occurred in the ovary when the ovum was prevented from escaping from the follicle due to various causes. Leopold[4], Gertsell[3], Russell and Black[8], Bittman[1], and Wollner[12] all suggested etiology based on various mechanical processes.

The physiological aspects have been brought up primarily by Rock's[7] excellent work on human conception. He emphasized that ovulation is the result of interplay among many complicated agents, stressing that hyaluronidase present in the sperm may be essential in dispersing the hyaluronic acid present in the granulosal and pellucidal layers of the ovum prior to fertilization. Blood serum has been reported to contain antihyaluronidase and since blood serum is commonly present in the vicinity of the ovum at ovulation the picture of fertilization is further complicated. Dr. Rock also mentions that viability of the ova and sperm and anatomic modifications of the ideal tubal fimbriae may be very significant in relation to fertility.

Report of Case

Mrs. M. S. R., a 36-year-old, withered, Latin-American woman, was first seen by one of us (O. H. H.) in September, 1950, for routine care during her sixth pregnancy. The last normal menses was in February, 1950, making her due date sometime in November, 1950. Her general past history was not remarkable. Obstetrically, she had had four uneventful deliveries, followed by the fifth pregnancy, terminated in 1946 by surgical excision of the right tube and ovary for an ectopic tubal pregnancy of two months' gestation. On initial examination in September of 1950 she seemed normally pregnant at six to seven months' gestation. Routine laboratory tests were normal. The pregnancy had been complicated by scant vaginal bleeding and lower abdominal cramping throughout March, 1950. This had been followed by left lower abdominal pain of intermittent "catchy" nature and associated with mild nausea and vomiting. In October of 1950 she had an episode of abdominal cramping diagnosed as false labor. On November 6, 1950, no fetal heartbeat was heard for the first time, although the patient insisted she felt movement of the baby.

In December, 1950, the senior author (W. F. B.) was called in consultation because of suspected intrauterine fetal death. At that time the abdominal size corresponded to an eight months' pregnancy. Further abdominal examination revealed a right sacrum posterior fetus with no fetal heart tone or placental souffle audible and no active fetal movement palpable. The skull was quite easily felt at the superior pole of the abdominal mass as a "bag of bones" with obviously decreased fetal intracranial pressure and overriding of skull bones. Death of a postterm fetus of intrauterine position was diagnosed and hospitalization for further observation and induction of labor advised. On Jan. 11, 1951, the patient finally consented to hospitalization, and at this time the previous findings were confirmed. The blood pressure was 140/90. No edema of face or extremities was noted. Vaginal examination revealed a very soft but uneffaced and undilated cervix pointing acutely posteriorly. A mass the size of a tennis ball seemed to lie high in the posterior pelvis. Laboratory tests showed the urine to be acid, specfic gravity 1.022, and with a trace of albumin and many granular and hyalin casts. The red blood count was 2.1 million with hemoglobin 47 per cent. The white blood count was 9,200 with 91 per cent polymorphonuclear cells, 8 lymphocytes, and 1 mononuclear cell. The blood was

type A, Rh positive. The diagnosis was pregnancy, intrauterine, two months post term, with a dead fetus, and complicated by uterine leiomyomas, anemia, and possible renal disease. Whole blood was obtained for transfusion and two rounds of Pitocin induction were given. The inductions were most marked by absolute failure to cause a single "uterine cramp." Consequently, since vaginal examination had precluded the feasibility of induction by artificial rupture of the membranes, cesarean section and probably cesarean hysterectomy were planned and prophylactic penicillin started.

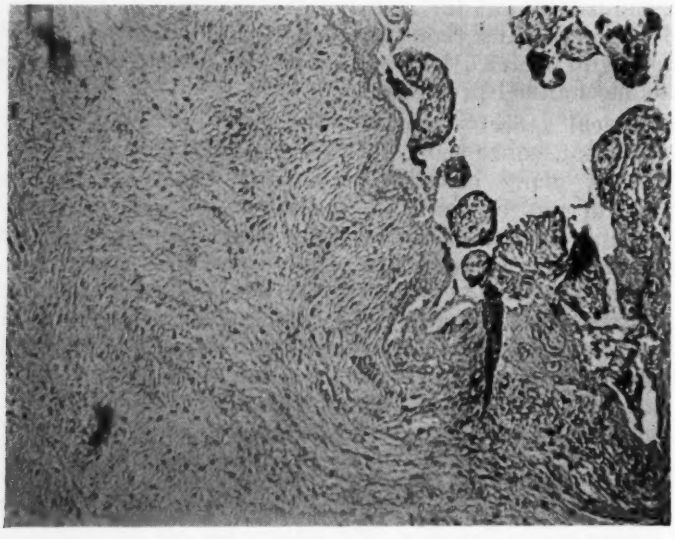

Fig. 1.—Photomicrograph of anterior sac wall near lower pole of ovary. Upper right, area showing placental tissue. Intermediate zone, decidual-type cellular reaction in ovarian tissue. Lower left, fibrotic ovarian tissue.

On Jan. 12, 1951, under spinal anesthesia the old abdominal scar was excised and the abdomen entered. Many omentoperitoneal adhesions in the old scar area were lysed. The tumor mass then exposed was the size of an eight months' uterus and was retroperitoneal except for the lower half which was attached to the uterus by the ovarian ligament. The left transverse and descending colon crossed this cystic tumor mass anteriorly, dividing the mass into almost equal upper left lateral and lower right medial halves. The left tube was grossly normal although stretched out over the lower surface of the tumor mass, now recognized as left ovary. The right tube and ovary were absent from previous surgery. The uterus was slightly enlarged and contained several small intramural leiomyomas. The left ovary was a leathery bag containing an obviously dead fetus of term size in right sacrum posterior position. The ovarian wall was thick, nodular, and variegated in color sufficiently to cause suspicion of coincidental ovarian cystadenocarcinoma. Because of the possibility of malignancy the abdominal incision was enlarged to allow removal of the mass in toto. By very tedious blunt dissection the ovary and its contents were freed and then removed intact and without hemorrhage. Total hysterectomy, left salpingectomy, and appendectomy were then done in addition, without event. Six hours postoperatively, the patient received 1,000 c.c. of whole blood for moderate shock, following which she promptly developed a severe hemolytic transfusion reaction accompanied by almost complete anuria for 24 hours. The red blood count and hemoglobin dropped to 1.9 million and 29 per cent, respectively, requiring another 1,000 c.c. of whole blood to bring the red blood count to 3.16 million with hemoglobin of 61 per cent. By the third postoperative day urine output was again normal and severe clinical jaundice had developed. Penicillin therapy was continued postoperatively until discharge on the tenth postoperative day. The highest temperature recorded was 100.4° F. She was discharged from the hospital on oral iron medication.

On Feb. 13, 1951, the patient was seen in the office with a red blood count of 4.86 million and hemoglobin 81 per cent. Voided urine showed a trace of albumin with 1.007 specific gravity and was otherwise negative. The patient had no complaints and was in satisfactory general health.

Specimen.—

Gross: The intact ovary and contents weighed 10 pounds, 3 ounces. The fetus alone weighed 8 pounds, was moderately discolored, seemed normally developed, and was markedly well preserved for having been dead two months. The cord was edematous, moderately discolored, and centrally implanted on the placenta. The placenta was large, being 17 cm. by 20 cm. by 4 cm. It lay anteriorly in the ovarian sac and the placental infarcts simulated the appearance of ovarian malignancy. The placental vessels were nonfunctional and almost no bleeding occurred on cutting them. Amniotic fluid was yellowish brown and very scant in amount. The uterus showed several small intramural leiomyomas and a markedly thickened endometrium. The left tube was grossly normal.

Microscopic: Multiple sections of tissue were taken at various sites in the tumor wall. Section at the lower pole of the anterior-lying placenta revealed a mass of decidua-like and placental tissue which had undergone necrosis, attached to a portion of ovary showing fibrotic connective tissue proliferation. Another section of the posterior tumor wall revealed fibrosis of ovarian tissue and pigment deposition in macrophages. No muscular elements were noted in any portion of the tumor sac. The uterine endometrium showed marked decidual reaction.

Pathological Diagnosis.—Primary ovarian pregnancy, left, extrafollicular, post term.

Summary

1. Ninety cases of ovarian pregnancy, including one case presented herein, have been reviewed.

2. The average woman afflicted with ovarian pregnancy is 30 years of age, has probably been a sterility case for a variable number of years, and frequently has had previous miscarriage or ectopic pregnancy.

3. The signs and symptoms of ovarian pregnancy are usually indistinguishable from those of ectopic pregnancy in general.

4. Seventy-five per cent of these pregnancies will be terminated by the end of the first trimester, while 25 per cent will last into the second trimester, of which half will last to the third trimester or beyond. Approximately 66 per cent of the viable fetuses will be stillborn and 18.2 per cent of these viable fetuses will be malformed.

5. The incidence of authentic cases reported in the literature is rapidly increasing, the actual number probably being much greater than supposed.

6. The ratio of ovarian to other extrauterine pregnancies is approximately 1 to 117, wihle the ratio of ovarian pregnancy to intrauterine pregnancy is approximately 1 to 25,000.

7. Slight revision and modification of the criteria of ovarian pregnancy have been offered.

8. Simplification and standardization in the classification of ovarian pregnancy have been suggested.

9. The etiology of ovarian pregnancy has been briefly mentioned with emphasis on the physiological basis of ovarian pregnancy causation.

We wish to express our gratitude to Drs. A. B. Cairns and E. E. Baden for their helpful suggestions and criticisms.

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UTERODYNAMICS IN PREGNANCY AND LABOR, WITH SPECIAL REFERENCE TO CALCIUM AND QUININE

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THE work of Ivy[1] on the physiology of the uterine musculature in pregnancy and labor aided greatly in developing a system for recording the status of patients before and during labor. He stated that "histologically and from the viewpoint of comparative embryology, physiology and anatomy the uterus pregnant and nonpregnant is divided into three parts: the corpus uteri or upper segment; the isthmus uteri or lower segment; and the cervix. Thus, the correlation of these known facts practically establishes Aschoff's divisions of the human uterus." Ivy further stated that "the four major properties of the uterine musculature are the same as those possessed by smooth muscles in general. First: contraction; second: relaxation; third: adjustment in length without change in intra-uterine tension; fourth: coordination."

Intrauterine pressure is developed equally throughout and force is exerted on the contents of the fundus, causing the presenting part of the fetus to descend and be maintained tightly against the cervix. The contraction wave is then followed by a period of relaxation during which intrauterine tension is continued but the musculature is able to return to its original chemical state and thus prepare itself for the following contraction.

Metrostasis is a relative fixation of the length of a muscle fiber at which it contracts or relaxes (Ivy[1]). Two terms are used to illustrate this action: (1) mecystasis, an increase in length of the muscle fibers at which they manifest resistance to stretch, meanwhile maintaining the ability to contract and relax without a change in tension; (2) brachystasis, a decrease in length of the fibers at which they manifest resistance to stretch, contract and relax without a change in tension.

Metrostatic adjustments probably begin as early as the twenty-second week of pregnancy when actual growth of the uterine fiber ceases and it develops the property of mecystasis which permits the uterine cavity to enlarge to accommodate the growing fetus without changing intrauterine tension.

Metrostatic adjustments of the uterine fibers gradually develop until term and the uterus is then ripe, and these properties are present to their greatest extent. Brachystasis is predominant in the fundus uteri, gradually diminishing toward the lower uterine segment and finally disappearing in the cervix, whereas mecystasis is the complete reverse and exhibits its maximum effect in the cervix.

These adjustments are inversely proportional to each other as demonstrated in Fig. 1.

The mecystasis present in the cervix can be detected by palpation as revealed by softening, effacement, and dilatation and will be found to be in direct proportion to the brachystatic adjustment present in the fundus.

This ratio is present throughout the entire ripened uterus with the exception that the anterior surface is dominant in brachystasis thus protecting the usual placental site, which maintains a diminished contractile ability throughout the posterior uterine surface.

Reynolds, Hellman, and Bruns,[2] using a multichannel tokodynamometer, revealed that dilatation of the cervix is associated with a gradient of diminishing physiological activity from the fundus to the lower uterine segment.

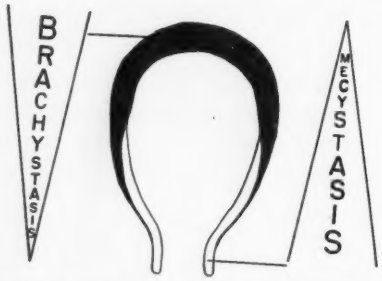

Fig. 1.—Brachystasis, represented by black, is dominant in the fundus and diminishes as it approaches the lower uterine segment and cervix. Mecystasis is dominant in the cervix and rapidly diminishes toward the lower uterine segment.

Uterine contraction waves (Ivy[1]) apparently originate in the region of the tubal portion of the myometrium and proceed in enlarging concentric waves of contraction which, after meeting in the midline, produce longitudinal shortening of the uterus, maintaining their greatest force in the anterior fundus. Very shortly, peristaltoid circular contractions begin, which probably are of value in maintaining the longitudinal position of the fetus by preventing the uterus from expanding laterally similar to a flattened toy balloon. These waves are brachystatic in type because the muscle fibers shorten and maintain this decrease in length without changing tension, thus causing progressive descent of the fetus without injury from increased intrauterine pressure. At the same time mecystasis causes the fibers in the lower uterine segment and cervix to relax and maintain their increased length without a change in tension and progressive dilation or dilution of the cervix is maintained. This is the physiological basis for the dominance of the fundus in normal labor. The cervix is not dilated but is actually pulled open by the shortening of the muscles of the fundus exerting a retracting force on the lower uterine segment and especially the anterior cervical lip, while the posterior portion of the cervix is maintained dorsally by the musculofascial attachments and a weaker fundus contraction. As the fetus progresses downward, the slack in the upper portions is taken up by brachystasis in the fundus.

After delivery of the fetus brachystasis becomes greatly exaggerated until the uterus is tightly contracted around the placenta and as rhythmical contractions again develop the placenta is expelled and the placental sinuses closed.

The property of metrostasis of the uterine muscle is not completely present before term (e.g., Braxton Hicks contractions) and, therefore, an unripe uterus is one in which progressive contraction waves with the ability to expel the uterine contents are not present. Metrostasis is not an inherent characteristic of uterine musculature, but develops and increases in a pregnant uterus as it approaches term, being complete and fully efficient at the time which is commonly spoken of as ripe. In patients with premature rupture of the membranes or others in whom labor has commenced with a firm cervix, prolonged labor accompanied by ineffectual contractions is frequently observed. These uteri do not exhibit true metrostatic adjustment. It is in this type particularly that calcium can manifest its greatest benefits.

Interest in the use of quinine and calcium in labor was revived as a result of a publication by Johnson,[3] who found that the stimulating effect of calcium upon uterine motility could be enhanced by quinine. In order to evaluate and confirm this observation, it was necessary to develop a plan which would aid us in evaluating the patient whose uterine musculature required the use of calcium. Each cubic centimeter of the calcium-quinine* preparation employed contains 0.06 Gm. of quinine gluconate (equivalent to 0.037 Gm. of anhydrous quinine base) and 0.009 Gm. of calcium ion.

Henkel[4] employed calcium and quinine in one hundred cases of abortion. He concluded that it was of no value to initiate and maintain adequate intensity of uterine contractions before the fourth month of pregnancy but gradually increased in efficiency after that time.

Piero Cattaneo[5] observed the progress of labor in twenty-three patients who had uterine inertia with early rupture of the membranes. The inertia was treated with intravenous injections of quinine-calcium. The average duration of labor after use of the drug was eight and one-half hours. Danforth and Ivy[6] concluded that calcium is necessary for maintenance of the tone, contractility, and co-ordinated activity of the postpartum uterus of the dog and rabbit. When the available calcium is sufficiently reduced by the use of soluble sodium hexametaphosphate, uterine contractions do not occur. Hart and Noble[7] concluded that calcium salts alone or in combination with small amounts of quinine are useful in initiating contractions in patients with ruptured membranes. Patton and Mussey[8] reported that calcium will increase the intensity of uterine contractions, is useful in stimulating the uterus in cases of inertia in the first or second stage of labor, but is not expected to overcome severe dystocia.

In our series of cases these statements were verified, but it was decided that some suitable system for establishing the status of a patient at term or in early labor should be developed. Adequate information can be derived from rectal examination and a five-point system was developed as follows:

Point I: Descent of the fetal head or presenting part by use of DeLee's classification (Fig. 2) and measurement in centimeters above or below the ischial spines.

*Known as Calgluquine and furnished by Sandoz Pharmaceuticals, San Francisco, Calif.

Point II: Position of the cervix. The normal position for this part a few weeks before term is backward and up in the hollow of the sacrum but as the process of ripening develops it gradually rotates in an arc toward the axis of the vagina. This arc has been arbitrarily divided into four parts and labeled, using I as the highest and most posterior position and IV when it is found directly facing the vaginal orifice (Fig. 3).

Point III: Effacement is found developing as the cervix gradually rotates and it is described in percentage of the normal one and one-fourth inches in length.

Point IV: Cervical dilatation measured in centimeters.

Point V: Consistency. Described by Calkins[9] as varying from firm, like the feel of cartilage in the nose, to soft as the lower lip.

All patients are examined rectally once a week, usually commencing four weeks before the confinement date, and the five points noted on the chart. Exception is usually made in any case where a low placental implantation is suspected.

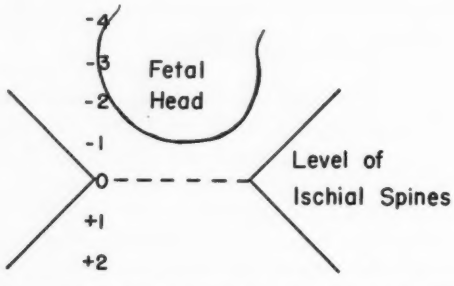

Fig. 2.—Descent of fetal head in relation to ischial spines.

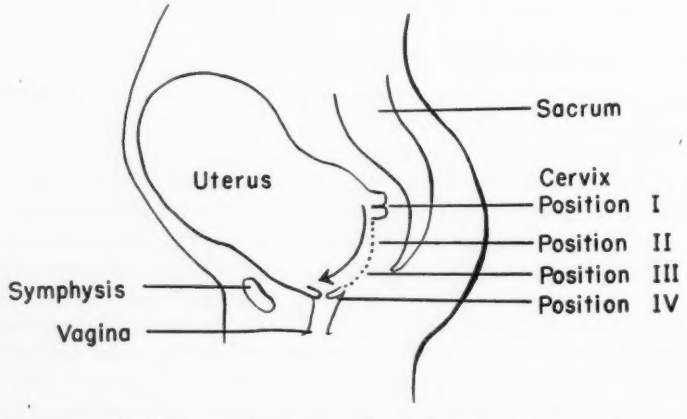

Fig. 3.—Arrow reveals rotation of cervix from posterior to anterior positions associated with effacement and dilatation.

If these facts are carefully noted, a truly ripened uterus with the fully developed properties of metrostasis can be detected before the onset of labor.

The use of these five points is a great help in evaluation of patients in labor who have been classified as having uterine inertia or cervical dystocia; also, those with premature rupture of the membranes who do not respond to stimulants or oxytocics present an almost constant pattern which reveals the five points to be head, III or higher; cervix I or II, markedly posterior; effacement, 10 to 30 per cent; dilatation, 0; and consistency, firm. Essentially all of these findings can be attributable to a lack of metrostatic adjustment.

Calgluquine was used as a routine procedure in this type of case with the development of uniform expulsive contractions increasing in quality and quantity and with softening and rotation of the cervix with subsequent dilation and expulsion of the uterine contents.

Winkler and Vetter[10] reported that regular and strong labor contractions developed in patients with contractionless or feeble labor after injection of Calgluquine.

One of the most spectacular uses of Calgluquine is in the postpartum hemorrhage of uterine inertia, for here, again, is a condition of lack of metrostasis. We use 10 c.c. intravenously with an immediate firm uniform contraction of the uterus. It was also noted that the action of oxytocics, such as Methergine, a semisynthetic ergot derivative, was greatly enhanced by calcium. Sandin and Hardy[11] reported the successful use of Neo-Calglucon 20 per cent solution (calcium gluconogalactogluconate) intravenously, following the use of Methergine after the third stage of labor, resulting in a reduction of blood loss. Methergine has proved, in our experience, confirmed by many observers, to have a more prompt and sutained action on the uterus than natural ergonovine. During the past ten years I have not found it necessary to pack a uterus for uncontrollable bleeding due to inertia.

TABLE I

			LABOR			MEMBRANES			CERVICAL DILATATION		LENGTH OF LABOR	
NO.	PRIMIPARAS	MULTIPARAS	INDUCED	SPONTANEOUS	INERTIA	INTACT	SPONTANEOUS RUPTURE	ARTIFICIAL RUPTURE	1.0 CM.	2.0+ CM.	PRIMIPARAS	MULTIPARAS
100	40%	60%	65%	27%	8%	16%	24%	60%	70%	30%	8.9 hours	7.4 hours

Material

A series of 100 cases in which Calgluquine was used at Swedish Hospital during the year 1948 was taken for study. While our experience with Calgluquine covered more than 1,300 cases, we chose 100 cases for evaluation. However, the five-point system of recording the characteristics of the cervix was not available on the patients' hospital charts for that year. The average length of labor in primiparas was 8.9 hours and in multiparas 7.4 hours, while 70 per cent of the cervices were not more than 1.0 cm. dilated. Induction of labor was performed in 60 per cent of the cases. The technique included two hot enemas at thirty-minute intervals with an intramuscular injection of 5 c.c. Calgluquine with the last enema and 5 c.c. in one-half hour. Pituitrin, ½ minim, is frequently used for two to four doses. The membranes are ruptured after labor is established. Two patients in the series developed uterine inertia with postpartum hemorrhage, which was controlled with 10 c.c. of Calgluquine intravenously. One of these did not receive Calgluquine before delivery.

The first stage of labor cannot proceed in a normal manner unless the uterus has acquired a metrostatic mechanism. The extrinsic nerves and the uterovaginal ganglion are not necessary for the initiation and progress of labor because they may be destroyed without interfering with the onset and progress of labor.

In the majority of patients, the approach of term or ripening may be determined by the five-point system of rectal examination. This method is also of value in determining whether the labor is true or false.

Calcium is necessary for tone and motility and has been used to assist in ripening the uterus and in overcoming uterine inertia. Calcium augments and co-ordinates uterine motility and quinine increases its sensitivity.

This series includes patients of several attending obstetricians. That the number of inductions is relatively high may be attributed to the fact that Calgluquine is an important agent in our technique. Our total hospital deliveries for 1948 were 2,861 and during the following three years Calgluquine was used in 1,281 cases from a total of 6,015 cases.

Summary

1. Careful study of the cervix by palpation will demonstrate whether or not metrostasis is fully developed. This system may be used for differentiating false from true labor.

2. Fully developed metrostatic adjustment is always present in a ripened uterus. Metrostasis is essentially impossible in the absence of calcium.

3. Uterine inertia may be overcome by the use of Calgluquine.

4. Calcium increases the response of the uterus to oxytocics.

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STUDIES ON Rh

I. Evaluation of Antihuman Globulin Serum in the Hemolytic Disease of the Newborn

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LEVINE[1] has made the statement, "It is not possible to predict the outcome of the infant on the basis of antibody studies alone." However, on considering the pathogenesis of hemolytic disease of the newborn, it seems that prenatal prognostication of fetal involvement should be possible, particularly if we consider the erythrocyte destruction in the fetus which seems to be one of the end products of antibody production in the mother.

Page and associates[2] listed five factors which they felt were important in the antenatal prediction of the degree of disease. These were: (a) presence of "blocking" antibodies; (b) significant quantity of antibodies; (c) antibodies more than ten weeks prior to delivery; (d) antibodies in every successive test; (e) ABO incompatibility.

Review of their statistics revealed: When all factors were present, twenty-six out of twenty-eight infants were affected. If two factors were absent, all babies were normal. When one factor was absent, twenty-eight out of thirty babies escaped the disease. These authors were primarily evaluating antibody activity in its relationship to hemolytic disease of the newborn.

At the United States Army Hospital, Fort Benning, Georgia, in addition to saline and albumin antibody determinations, the antihuman globulin serum described by Coombs and co-workers[3] is routinely used to determine the presence and titer of antibodies in the mother.*

The purpose of this report is to discuss the value of the use of the antihuman globulin serum and the experience we have had in attempting prenatal prognostication of the degree of hemolytic disease.

Material and Method

This study covered a period from Feb. 1, 1951, through Feb. 29, 1952. During this time there were 1,883 deliveries. All mothers had a slide test for

*Sacks[6] has suggested that for purposes of clear differentiation the antibody be identified by the medium in which its activity can be detected. We have followed this suggestion and will refer to saline and albumin antibodies as those antibodies demonstrated in those respective media. Further, we are anxious to use these terms since they are the terms most generally used and understood by obstetricians. The antiglobulin test was more difficult to label since two sets of media are used, but since the test is conducted with antihuman globulin serum this somewhat awkward term will be used in this presentation.

Rh[4] and ABO types, and the tube test for Rh factors (C, D, and E).[5] Rh-negative bloods were then checked by the tube technique for the Hr factors (c and e).[5] All Rh-negative patients returned and were rechecked to rule out any possibility of error.

Determination of antibodies included the testing for saline, albumin, and antihuman globulin serum antibodies. Titers were performed at four-week intervals from the first visit to the thirtieth week, at two-week intervals to the thirty-sixth week, and weekly thereafter. When apparently significant sensitization was occurring, as indicated by rising titers, more frequent determinations were done.

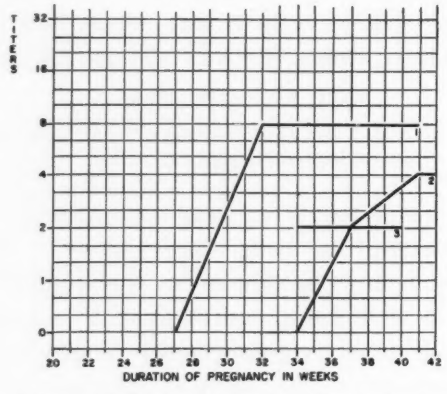

Fig. 1.—Albumin antibody titers of patients in Group I (no other antibodies were demonstrated in this group).

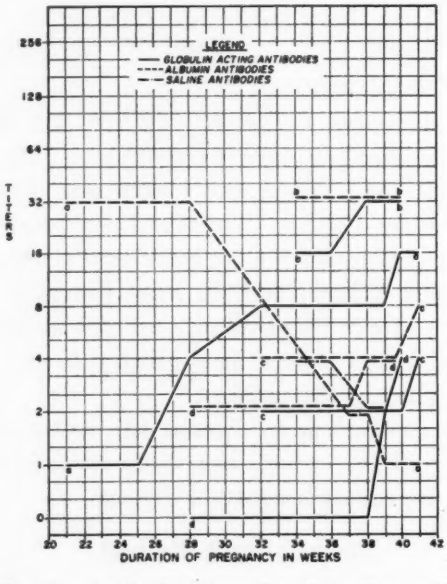

Fig. 2.—Antibody titers found in Group II.

At the time of delivery infants were carefully studied. Hematological data were obtained on both cord and capillary bloods, which included red blood count, hemoglobin, smears for blood morphology, Rh and ABO types, Coombs test, and icteric index where indicated. The pediatrician was called to give a clinical impression of the infant.

Results

Three hundred sixteen mothers were Rh negative; fourteen demonstrated antibodies. In reviewing the statistics on the fourteen mothers with titers, they fell into three groups:

Group I.—No antihuman globulin serum antibodies, 3 cases (Fig. 1 and Table I).

TABLE I. GROUP I. BLOOD PICTURE ON INFANTS

INFANT	GESTATIONAL AGE		COOMBS	Rh TYPE	BLOOD TYPE	RED BLOOD CELLS	HEMOGLOBIN	NUCLEATED RBC PER 100 WBC
1	40	Cord	0	CDe	–	4.3	14	2
		Capillary	0	CDe	–	4.3	14.5	0
2	43	Cord	0	CDe	A	3.5	10.9	0
		Capillary	0	CDe	A	4.0	11.4	0
3	41	Cord	0	cDE	O	3.9	13.0	2
		Capillary	0	cDE	O	5.8	18.3	0

No antihuman globulin serum or saline antibodies were present. Only low albumin antibody titers, ranging from 1:1 to 1:8, were demonstrated. All of the infants were normal; the Coombs tests were negative. The blood findings of the newborns were considered to be within normal limits.

Group II.—Low titer of antihuman globulin serum antibodies without a sharp rise, 4 cases (Fig. 2, Table II).

TABLE II. GROUP II. BLOOD PICTURE ON INFANTS

INFANTS	GESTATIONAL AGE		COOMBS	Rh TYPE	BLOOD TYPE	RED BLOOD CELLS	HEMOGLOBIN	NUCLEATED RBC PER 100 WBC
A	41	Cord	+	cDE	A	4.1	14.7	5
		Capillary	+	cDE	A	5.3	15.1	1
		Day 1				5.5	18	
B	40	Cord	+	cDE	O	3.8	12.7	29
		Capillary	+	cDE	O	4.0	13.0	13
		Day 1				4.0	13.5	11
		Died—pneumonia and atelectasis						
C	40	Cord	–	CDe	A	4.0	13.9	16
		Capillary	–	CDe	A	4.4	15.1	2
		Day 1				4.5	16.5	
D	40	Cord	–	CDe	O	4.6	14.7	10
		Capillary	–	CDe	O	6.0	20.0	2
		Day 1				7.8	24.0	1

All 4 mothers had positive albumin and antihuman globulin serum titers; one also had positive saline antibodies (Case B). Case A was interesting for

the albumin titer dropped as gestation advanced. The antihuman globulin serum antibodies rose slowly but did not reach a significant level. (Further study is being done on just what might be considered a significant titer.) Up to the present we have felt that a titer of between 1:32 to 1:64 is significant. A low titer up to 1:8 over an eighteen-week period was not harmful to the infant. Two infants (A and B) had positive Coombs tests. Antihuman globulin serum antibody titers in Case A rose to 1:16 just prior to term and 1:32 in Case B. Albumin antibody in A dropped from 1:32 to 1:1, while in B it remained at 1:32 during our observation.

Two infants (C and D) had a negative Coombs test. Neither albumin nor antihuman globulin titers rose over 1:4 in the mothers of these infants.

Group III.—Sudden, sharp rise in titer of antihuman globulin serum antibodies, 7 cases (Figs. 3 and 4, Table III).

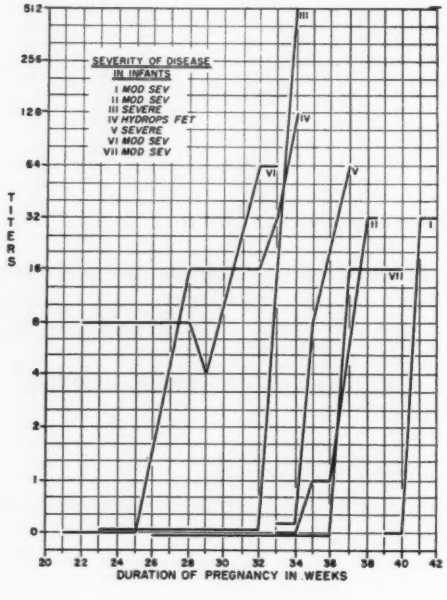

Fig. 3.

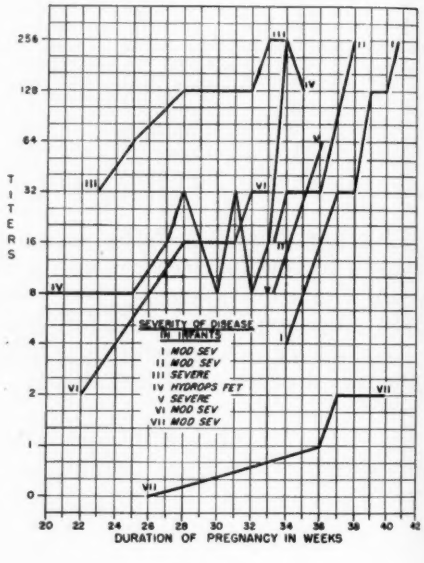

Fig. 4.

Fig. 3.—Globulin-acting antibody titers of patients in Group III.
Fig. 4.—Albumin-acting antibody titers of patients in Group III.

This group was of particular interest. First, in each case there was a sudden, sharp elevation in the antihuman globulin serum and fairly high albumin antibody titers. The rise in antihuman globulin serum antibodies ranged from three- to ten-tube dilutions and occurred within a relatively short period of time, three weeks or less. Second, every infant had a moderately severe or severe degree of hemolytic disease of the newborn. All were Coombs positive.

Cases 1, 2, and 7 revealed moderately severe evidence of the hemolytic process; Cases 3, 4, 5 and 6 were severely affected. The following is a brief summary of the severely affected group.

CASE 3.—History of neonatal death of sibling secondary to hemolytic disease of the newborn. Mother had had a previous cesarean section. A repeat cesarean section was done in the thirty-fourth week because of a rapidly rising antihuman globulin serum antibody to 1:512 with associated rise in the albumin antibody titer. Exchange transfusion

was given to the baby immediately after delivery. The infant is now living and well at the age of 8 months.

CASE 4.—History of neonatal death of sibling secondary to hemolytic disease of the newborn. There was a sudden rise of the antihuman globulin serum antibody between the twenty-fifth and twenty-eighth weeks, a leveling off, and a second sharp rise to 1:128 with fetal death in utero in the thirty-third week. Five days later the patient delivered a stillborn infant with hydrops fetalis.

CASE 5.—There was a sudden rise of the antihuman globulin serum antibody just prior to the thirty-eighth week. Labor was induced. The infant had marked anemia but was not transfused. He is now living and well at the age of 7 months.

CASE 6.—There were two living siblings with no history of hemolytic disease of the newborn. The mother had an antihuman globulin serum antibody titer of 1:8 when first seen. She developed a sudden rise to 1:64 between the twenty-ninth and thirty-second weeks. Labor was induced in the thirty-third week. The infant had considerable anemia and died fifteen hours after delivery despite an exchange transfusion. Autopsy findings revealed prematurity, atelectasis, and erythroblastosis fetalis.

It was noted that when the sudden rise in antihuman globulin serum occurred prior to the thirty-sixth week, the infants had severe hemolytic disease.

TABLE III. GROUP III. BLOOD PICTURE ON INFANTS

INFANT	GESTATIONAL AGE		COOMBS	Rh TYPE	BLOOD TYPE	RED BLOOD CELLS	HEMOGLOBIN	NUCLEATED RBC PER 100 WBC	ICTERIC INDEX
1	42	Cord	+	CDe	O	4.4	13.9	13	
		Capillary	+	CDe	O	4.4	13.0	10	
		Day 1				3.9	12.3		
2	38	Cord	+			6.0	1.5	132	50
		Capillary	+				3.8		
		Day 1				12.7	2.8	14	
3	34	Cord	+	CDe	B	4.2	14.5	35	40
		Capillary	+	CDe	B	4.2	13.5	15	
			Exchanged						
		Day 4				5.2	14.3		
4	34		Hydrops fetalis						
5	37	Cord	+	cDE	O	1.34	4.0	240	30
		Capillary	+	cDE	O	6.3	4.0	210	95
		Day 1				4.22	13.5		
6	33	Cord	+	CDe	A	2.8	12.3	88	
		Capillary	+	CDe	A	3.5	13.9	31	
			Exchanged			6.0	16.4	40	
			Died atelectasis, prematurity, erythroblastosis fetalis						
7	40	Cord	+	CDe	A	3.2	9.6	9	
		Capillary	+	CDe	A	4.6	15	5	
		Day 2				3.2	11.3	3	

Comment

Sacks[6] has stated that the saline antibody titer was not informative. In this study there was no correlation between the severity of disease in the newborn and the saline antibodies.

The albumin antibodies showed a very close correlation to the severity of the disease. However, the rise and duration of the titer were sometimes misleading.

The antihuman globulin serum antibodies were more directly related to the severity of the disease than the others. We used it not only to predict fetal outcome but also to predict the time when sensitization was becoming significant. The absence of the antihuman globulin serum titer was always correlated with a negative Coombs test in the infant. The presence of the antihuman globulin serum titer was associated with a positive Coombs test in the infant only when the titer was more than 1:4.

We were impressed by the observation that a rapid rise in the antihuman globulin serum titer was accompanied by disease in the infant. The earlier the rise, the greater was the risk to the infant. A titer of 1:32 to 1:64 was considered significant.

Summary

1. The study covered a period from Feb. 1, 1951, through Feb. 29, 1952. During this time there were 1,883 deliveries. Three hundred sixteen mothers (16 per cent) were Rh negative; fourteen (4.4 per cent of Rh-negative mothers) were sensitized.

2. There was a closer correlation between the degree of hemolytic disease of the newborn and the antihuman globulin serum titer than with the albumin or saline titer.

3. A sudden high rise in antihuman globulin serum titer was a warning of difficulty in the infant. The earlier the rise, the greater was the probability of damage to the infant.

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CLASSIFICATION OF FORCEPS OPERATIONS ACCORDING TO UNIFORM RADIOLOGICAL AND CLINICAL CRITERIA

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THERE is a considerable divergence of opinion regarding the definition of the various types of forceps deliveries. Adair, on behalf of the American Committee on Maternal Welfare, sent out a questionnaire on the definitions used for forceps operations, and the lack of uniformity and diversity of opinions lead to confusion and tend to vitiate any comparison of data collected from various sources.

Recently three classifications have been proposed in an attempt to standardize the terminology. American textbook authors, including Titus, Greenhill, McCormick, and Eastman, formulated a classification of forceps operations which they hoped would be simple, practicable with or without x-ray, and conducive to the safest possible management of the second stage of labor. Only three types of forceps are classified:

1. High forceps was defined as the application of the forceps before engagement has taken place, which they state is easy to demonstrate clinically by the fact that the presenting part has not yet reached the level of the ischial spines.
2. Low forceps was defined as the application of forceps when the head is visible, the skull is on the perineal floor, and the sagittal suture is in the anteroposterior diameter of the pelvis.
3. Midforceps was defined as the application of forceps before the criteria of low forceps have been met, but after engagement has taken place.

Many obstetricians would object to the definition of high forceps stated in the foregoing classifications because the presenting part may not have reached the spines and the greatest diameter of the head may be below the inlet and thus be fully engaged. This situation arises frequently because of the fact that the distance from the superior strait to the ischial spines is usually about 3 cm. greater than the distance of the vertex to the biparietal diameter in a flexed head. On the other hand, in extensions of the head such as face presentation, the biparietal diameter is further from the leading point than in the flexed positions. Hence, the level of the biparietal diameter is higher than would be expected in an occiput presentation with the leading point on the same level. The presenting part may, therefore, be at the spines and the head not fully engaged.

The chief objection to the definition of low forceps, as acknowledged by Eastman, has been that rotation to the anteroposterior diameter has been demanded. It is argued that rotation and station are not necessarily functions

of each other. A head may reach the same station: head visible, skull on the perineal floor, and may be in the direct occiput posterior position, and it may still be a difficult forceps delivery, especially for the novice.

This classification is almost suitable for the use of nurses who are in charge of limiting the activities of untrained physicians to low forceps, but neither may be able to determine the position.

The larger pelvic area covered by midforceps includes the entire pelvic depth from the spines to the perineum, which includes the high and low midforceps groups, and is considered undesirable by Dennen. The perineum is not a good landmark because it may be absent in complete tears, depressed in badly lacerated perinea and, moreover, is not visible by x-ray.

The second classification is that proposed by Dennen and is based on the relationship of the station of the head (biparietal diameter) to the four major planes of the pelvis. They are: (1) the plane of the inlet (superior strait) which is bounded by the promontory of the sacrum and the upper inner border of the symphysis; (2) the plane of greatest pelvic dimensions (midplane) which extends between the middle of the inner border of the symphysis and the junction of the second and third sacral vertebrae; (3) the plane of least pelvic dimensions (plane of ischial spines) which is bounded anteroposteriorly by the lower, inner border of the symphysis and the sacrococcygeal joint, and laterally by the ischial spines; and (4) the plane of the outlet, quadrilateral in shape, which is bounded by the sacrococcygeal joint, the ischial tuberosities, and the inferior border of the symphysis. The corresponding operative deliveries should be entitled high, mid, low mid, and low forceps.

A high forceps delivery is one in which the biparietal diameter is in the inlet or superior strait of the pelvis and the leading bony point of the head is just above the plane of the ischial spines. Anything higher should be labeled a forceps application to an unengaged head.

A midforceps delivery is one done on a head, the leading bony part of which is at or just below the plane of the ischial spines, with the biparietal diameter below the superior strait. The head nearly fills the hollow of the sacrum.

A low midforceps delivery is one in which the biparietal diameter is at or below the plane of the ischial spines, with the leading point within a fingerbreadth of the perineum between contractions. The head completely fills the hollow of the sacrum.

A low forceps delivery is one in which the bony head is on the perineum between contractions and is visible during a contraction. The biparietal diameter is judged to be below the plane of the ischial spines with the sagittal suture in or nearly coinciding with the anteroposterior diameter of the outlet.

Very few obstetricians actually do palpate for the biparietal diameter or can locate it accurately, especially in the molded or asynclitic head. This classification being based on the biparietal diameter's location, the clinical classification by vaginal examination is either not made or is inaccurate in many cases. A second objection to this classification is that the posterior terminus of the

plane of least dimensions and of the outlet are identical but the forceps deliveries from these locations are classified as low midforceps and low forceps, respectively. The use of bony landmarks for the midpelvis and inlet and the soft tissue perineum for low midpelvis and outlet is illogical. The classification should, in my opinion, not be based on the excursions of the presenting part with contractions. The contractions may be absent because of uterine inertia or because of the influence of anesthesia, especially of the regional type. Because of variations in pelvic size and architecture, the plane of least dimensions may not always be below the plane of greatest dimensions. Moreover, the classification includes the distinction whether the head fills the hollow of the sacrum completely or not. Very often there is no hollow and a straight sacrum exists.

The third classification which appears to eliminate the preceding objections has recently been proposed by Weinberg. The definition of a type of forceps operation must include reference to a fetal and a pelvic plane which are ascertainable and constant.

For the fetal point of reference the use of the biparietal diameter is not wise because in the average obstetric forceps operation the operator contents himself with the station of the most dependent portion of the presenting part and the location of the sutures and fontanels for determining position and station.

The location of the biparietal diameter is easily determined by a lateral x-ray but its level in the pelvic axis by manual examination is difficult.

At an open meeting I asked forty qualified obstetricians if they felt for the level of the biparietal diameter when doing midforceps deliveries and only one said that he did; moreover, in a face or brow presentation, the biparietal diameter is not the greatest diameter involved in the mechanism of labor. Therefore, the use of the most dependent portion of the presenting part, excluding a caput succedaneum, is recommended. In like manner, the pelvic points of reference must be fixed and locatable either by x-ray or manually. Use of the ischial spines to designate the midpelvis and the perineum for the outlet is illogical because the perineum may be absent in third-degree tears or depressed in lacerated perinea in relation to the true pelvis; furthermore, the muscles are not discernible by x-ray.

The logical plane to select as the station of the outlet is the level of the ischial tuberosities, which are fixed and easily located by x-ray or manually. The plane of the inlet is, of course, the linea terminalis at the level of or slightly below the true conjugate. Therefore, the following definitions are suggested:

1. A high forceps delivery is one in which the leading bony point lies between the inlet and ischial spines and approaches the spines to such an extent that the presenting part is engaged. That is, its greatest diameter is below the inlet. The leading point usually is within 3 cm. above the spines. Any forceps operation higher than this would be to an unengaged head and would be termed a floating forceps.

2. A midforceps operation is an obstetric operation by which a fetus which presents cephalically and whose presenting part is located in the midpelvis, i.e., between the planes of the ischial spines and ischial tuberosities, is delivered by forceps.

3. A low forceps operation is one in which the leading point lies below the tuberosities.

4. An outlet forceps is one in which the presenting part is easily visible and is distending the perineum and vulva.

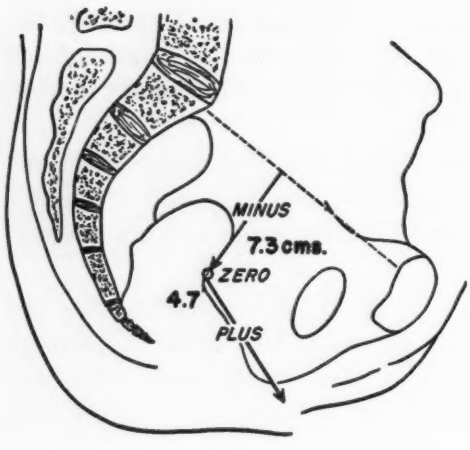

Fig. 1.

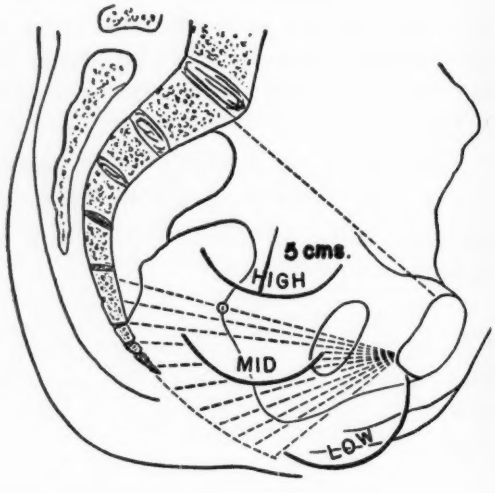

Fig. 2.

Fig. 1.—Stations of the birth canal. Station zero is at line drawn between ischial spines. Stations minus are above, and stations plus are below zero station. Numerals will represent centimeters in minus or plus stations. (From Weinberg, Arthur: Am. J. Surg. 83: 143, 1952.)

Fig. 2.—Areas of high, mid- and low forceps applications. (From Weinberg, Arthur: Am. J. Surg. 83: 143, 1952.)

As shown in Figs. 1 and 2, the average distance from the vertex to the biparietal diameter in a flexed head is 5 cm., and the average distance in the pelvic axis from the inlet to midpelvis and from the midpelvis to outlet is 7.3 and 4.7 cm., respectively. Therefore, the station of the biparietal diameter can be estimated. By knowing the level of the ischial spines along the pelvic axis the position of the biparietal can be plotted by adding 5 cm. to the station of the most dependent position. The level of the spines may be relatively near or far from the pelvic inlet or outlet depending on the architectural features of the pelvis.

If the vertex is at the spines, the greatest diameter will be located as follows: The distance between inlet and spines measured by x-ray along the pelvic axis is 7.3 cm. and the distance from the vertex to the biparietal diameter is 5 cm.; therefore, the distance below the inlet of the biparietal diameter would be 2.3 cm. For example, if the vertex is at the ischial tuberosity, the biparietal usually is just above the spines by 0.3 cm. and the station is midpelvis.

Clinically, the determination of the station of the presenting part with the estimation of the station of greatest diameter is the method commonly

used and, if understood, should give all the information needed without taking an immediate lateral x-ray film.

Correction must be made for the influence of asynclitism, molding, and extension of cephalic presentations when present. Caput succedaneum is eliminated from the classification by limiting the designations to bony points.

Summary and Conclusions

In the interests of uniformity and accuracy, three recent classifications of forceps operations have been analyzed. The advantages and disadvantages of each have been discussed. From a clinical and radiological point of view, it would appear that the third classification based entirely on bony landmarks offers the least objections, gives accurate information and should be generally acceptable.

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STATISTICS OF BIRTHS IN THE UNITED STATES

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SOME statistical compilations and findings relative to births in the United States, incidentally afforded in connection with the study of another subject and perhaps not elsewhere or otherwise available, may be worthy of publication.

The material is derived from the natality statistics collected and annually published by the National Office of Vital Statistics, conducted under the United States Census Bureau to 1944, and since then under the Federal Security Agency. The publication of these birth statistics began in 1915, and covered the country only partially, the "registration area," until, in 1933, registration became complete for the entire country. From 1915 to 1948, the date of the latest published volume, the data included 75,148,134 live and dead births, which should afford a yardstick adequately representative in this field. The period 1933-1948, covering the entire country (43,212,423 births), is especially analyzed.

Further data are afforded by a brochure, "The Numerical Proportions of the Sexes at Birth," compiled by the writer from world-wide statistics of 707,-421,708 births, and published in the *Memoirs of the American Anthropological Association* (vol. 1, part 4, pages 245-300, 1907).

Total Births, Live and Dead.—From 1915 to 1948, inclusive, the number of live births registered in the United States was 73,050,353. Stillbirths were not published prior to 1922, except for the year 1918; but the figures for 1922-1948 were as follows:

Born alive	64,141,052
Stillborn	2,097,781
Total	66,238,833

The figures for 1933-1948 were:

Born alive	41,976,268
Stillborn	1,236,155
Total	43,212,423

The annual numbers of live births registered in the United States in recent years have ranged as follows:

1950 (estimated)	3,548,000	1945	2,735,456
1949	3,559,529	1944	2,794,800
1948	3,535,068	1943	2,934,860
1947	3,699,940	1942	2,808,996
1946	3,288,672	1941	2,513,427

Stillbirths.—The statistics of stillbirths are not completely satisfactory. One reason is that the official definition of stillbirth varies in different states and countries, as to the stage of gestation taken as the base; this impairs and

confuses the uniformity and comparability of the statistical reports. Another is that, for obvious reasons, especially avoidance of publicity or trouble, many cases are likely not to be reported, resulting in underregistration. The private or secret disposition of a dead fetus or infant, without publicity, can be accomplished more easily than of a living infant. Birth statistics have to be accepted as registered, with realization of the uncertainties.

The distinction between live births and stillbirths adopted and specified by the Office of Vital Statistics is as follows: "A fetus showing no evidence of life after complete birth (no action of heart, breathing, or movement of voluntary muscle) if the twentieth week of gestation has been reached, should be registered as a stillbirth." However, in some of the states, the registration of the stillbirths includes cases of less than 20 weeks' or 5 months' gestation; and these cases are included in the figures here presented.

The statistics of stillbirths in the United States for the period beginning in 1922 are presented in Table I. The figures show a continuous and gratifying reduction in the incidence of stillbirths in this country during the past three decades.

TABLE I. STATISTICS OF STILLBIRTHS IN THE UNITED STATES

Embracing mostly fetuses of at least 5 months' gestation, but including also cases of less than 5 months as registered in some of the states

Births, 1922-1948.—					
Born alive					64,141,052
Stillborn (3.17 per cent)					2,097,781
Total					66,238,833
Stillbirths per 1,000 live births					32.7
Births, 1933-1948.—					
Born alive					41,976,268
Stillborn (2.86 per cent)					1,236,155
Total					43,212,423
Stillbirths per 1,000 live births					29.4
Ratios of Stillbirths per 1,000 Live Births.—					
1922	39.4			1940	31.3
1925	38.1			1945	26.6
1930	39.2			1948	23.5
1935	35.8				
		1925-1929	39.0		
		1944-1948	25.2		

Ratio of the Sexes at Conception and Birth.—A yardstick for the analysis of the relative proportions of the sexes at conception and birth is afforded by the statistics of births in the United States, by sex, for 1933-1948, as presented in Table II.

The sum of the numbers of the live births and the stillbirths represents the ratio of the sexes, usually expressed as the numbers of males for each 1,000 females, at their initial conception and differentiation. For some unknown biological reason (perhaps through the evolution of a genetic trait fittest for survival of the race) males at conception exceed the females in number by upward of 6 per cent (1,060:1,000 in this series). After this start the stillbirths, which represent the intrauterine mortality, reduce the numbers to the sex ratios of the infants born living. It is well shown by statistics that the vitality, viability, and longevity of human females are greater than of males; the popular idea that the females are the weaker sex is belied by the facts. Accordingly, the intrauterine death rate of the male fetuses is much greater than that of the

females, upward of 25 per cent (1,266:1,000); and this disparity results in the normal proportion of the sexes as born alive. For instance, starting with a relative initial conception of 1,086 males and 1,024 females, the average of 31 male and 24 female stillbirths brings the ratio of live births down to 1,055 male and 1,000 female infants. It is noteworthy that the relative death rates of the two sexes is practically the same in the intrauterine period (1,266:1,000) as in the first year of life (1,279:1,000).

As the comparative statement in Table II shows, there is close agreement of the United States 1933-1948 statistics (of some 43,000,000 births) with a much larger series of world-wide statistics (of over 447,000,000 births); the lessening of stillbirths in the later period is also manifest.

TABLE II. STATISTICS OF BIRTHS IN THE UNITED STATES, BY SEX, 1933-1948
Not including cases in which the sex was not reported

	MALE	FEMALE	TOTAL
Live births	21,549,888	20,426,380	41,976,268
Percentage	51.33	48.67	100
Ratio	1,055	1,000	2,055
Stillbirths (intrauterine deaths)	628,439	496,394	1,124,833
Percentage of total births	2.83	2.37	2.61
Sex ratio	1,266	1,000	2,266
Sex percentage	55.87	44.13	100
Mortality in first year of life			
Sex ratio	1,279	1,000	2,279
Per cent	56.13	43.87	100
Total births, live plus dead; equals number at conception, or fifth month of gestation	22,178,327	20,922,774	43,101,101
Per cent	51.46	48.54	100
Sex ratio	1,060	1,000	2,060
Initial proportion at conception	1,086	1,024	2,110
Stillbirths	31	24	55
Born living	1,055	1,000	2,055

COMPARATIVE STATEMENT	NUMBER OF MALES PER 1,000 FEMALES BORN		
	LIVING	DEAD	TOTAL
World-wide aggregate, all races (447,019,579 births), to 1907	1,056	1,302	1,062
United States, 1933-1948 (above)	1,055	1,266	1,060

LIVE BIRTHS BY SEX AND RACE	TOTAL	WHITE	NEGRO*
Male	21,549,888	18,938,111	2,463,055
Female	20,426,380	17,883,413	2,400,529
Total	41,976,268	36,821,524	4,863,584
Number of sons for 1,000 daughters	1,055	1,059	1,026

*Nonwhite races other than Negro not included.

The number of infants born alive will be equal to the number originally conceived minus the intrauterine deaths, the stillbirths. In the general aggregate about 1,055 or 1,056 male infants are born alive for every 1,000 females. The number of live births will, however, vary with the number of stillbirths which may occur under different vital and hygienic conditions; and, the more the stillbirths, with their greater male fetal mortality, the less will be the proportionate number of male infants born alive. As an exemplification, while in the United States in 1933-1948 the total sex ratio for all races of live births was

1,055 males per 1,000 females, the rate was 1,059:1,000 for the white race, and only 1,029:1,000 for the Negro race. This can be attributed to poorer vital conditions causing increased fetal mortality among the Negro population. Another striking illustration is afforded by the ratio in illegitimate births, where the conditions are obviously decidedly adverse to fetal survival; a large statistical survey showed a general average of only 1,045 live male births to 1,000 female in this group. The low ratio of males in plural births is another illustration. In general, therefore, the relative number of live male births is an index of the associated vital and hygienic conditions; the lower the male rate, the worse are those surroundings, causing more stillbirths and fetal deaths.

TABLE III. PLURAL BIRTHS IN THE UNITED STATES, 1915-1948

Live births, total	73,050,353
Single births	71,471,683
Plural infants born alive	1,578,670
Plural births, in which at least one infant was born alive (totally stillborn sets not included in this section):	
Total number of cases (accouchements) of plural births	811,657
Single births	71,471,683
Total number of accouchements	72,283,340
Total number of plural infants	1,631,469
Born living	1,578,670
Stillborn (3.23 per cent)	52,799

NUMBER OF PLURAL CASES		NUMBER OF ACCOUCHEMENTS FOR EACH CASE
Twins	803,620	90
Triplets	7,921	9,126
Quadruplets	114	634,064
Quintuplets	2	?
Number of labors per total plural births	–	89
Total	811,657	
Proportion of plural cases (mainly twins) to total accouchements 1.12 per cent; annual range 1.01 to 1.18 per cent		
Incidence of plural births by race (1944-1948)		
White		96
Nonwhite		79
Incidence of plural births increases with age of mother, being highest in 35-39 year period		

QUADRUPLET BIRTHS	NUMBER OF CASES	BORN ALIVE	BORN DEAD	STILLBIRTHS PER CENT
All children born alive	78	312	0	0
At least one child born alive	114	414	42	9.2
All children stillborn	9	0	36	100.0
Total	123	414	78	15.9

Plural Births.—The statistics of plural or multiple births—styled "plural" births in the official reports—in the United States for the period of 34 years from 1915 to 1948 are presented in Tables III and IV, which are largely self-explanatory. The statistics are more fully presented for the plural births in which at least one of the infants was born living, than for the all-stillborn plural births.

As might be expected from the adverse vital conditions associated with overcrowding in the uterus, the incidence of stillbirths is increased in plural gestation and birth, the proportion increasing with the number of the multiplets. The total proportion of stillbirths in the plural cases (the vast majority of which are twins) in which at least one child was born alive was 3.23 per cent, which is slightly more than the contemporary 3.11 per cent for all births. However, if to this were added the figures for the plural births in which all the infants were born dead, the percentage of the stillbirths would rise materially, especially for the cases above twins. An illustration is afforded for the higher multiplets by the statistics for quadruplets. In this group the proportion of stillbirths in those cases in which at least one child was born alive was 9.2 per cent; but including the cases in which all the children were born dead the stillbirths amounted to 15.9 per cent.

TABLE IV. SEX DISTRIBUTION IN PLURAL BIRTHS

Twins (from various sources).—		
2 males	234,497 cases	32.7 per cent
1 male, 1 female	264,098	36.8
2 females	219,312	30.5
Total	717,907	100
Total number of males		733,092
Total number of females		702,722
Total number of infants		1,435,814
Number of males for 1,000 females		1,043
Triplets (from various sources).—		
3 males	1,786 cases	24.1 per cent
2 males, 1 female	1,970	26.5
1 male, 2 females	1,870	25.2
3 females	1,795	24.2
Total	7,421	100
Total number of males		11,168
Total number of females		11,095
Total number of infants		22,263
Number of males for 1,000 females		1,007
Quadruplets (United States, 1915-1948).—		
4 males	23 cases	20.2 per cent
3 males, 1 female	17	14.9
2 males, 2 females	26	22.8
1 male, 3 females	26	22.8
4 females	22	19.3
Total	114	100
Total number of males		221
Total number of females		235
Total number of infants		456
Number of males for 1,000 females		940
Quintuplets (miscellaneous cases).—		
5 males	10 cases	16.7 per cent
4 males, 1 female	8	13.3
3 males, 2 females	12	20.0
2 males, 3 females	10	16.7
1 male, 4 females	7	11.7
5 females	13	21.6
Total	60	100
Total number of males		145
Total number of females		155
Total number of infants		300
Number of males for 1,000 females		935

The relative number of male infants born per 1,000 females as shown in the statistics of the various categories of plural births may be summarized as follows:

Total born living	1,055
Twins	1,043
Triplets	1,007
Quadruplets	940
Quintuplets	935

This shows a sharp decline in the relative ratio of male births with the increase in the number of multiplets, and the associated intrauterine overcrowding. Increase in male fetal mortality thus involved should lower the ratio of males born alive. However, without complete statistics of the stillbirths, a reliable estimate of the ratio of the sexes at the initial conception cannot be assured; and it is possible that in plural gestations, for some unknown reason, the original differentiation of the sexes differs numerically from that in single births.

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LEPTOTRICHIA (LEPTOTHRIX) VAGINALIS

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THE first reference to the presence of a filamentous bacterium in the human vagina was that of Scanzoni in 1861.[1] He observed a very fine filament which he identified with the *Leptothrix buccalis* of Robin.[2,3] In 1895 von Herff[4] reported twenty-six cases of mycotic colpitis, sixteen of which he attributed to *M. albicans,* four to *M. candida,* four to cause unknown, one to a Saccharomycete, and one to *Leptothrix vaginalis.* He described this last organism as a nonbranching, segmented, narrow-thin, water-clear filament staining with iodine. He further stated that these organisms were gathered among fine granular detritus and formed grayish somewhat mucoid masses lightly deposited on a slightly inflamed mucous membrane and easily wiped off. He stated that symptoms were lacking.

In 1933 Starck[5] reported on three cases of Leptothrix of the vagina. The patients, two of whom were pregnant, were seeking advice because of a severe discharge which showed a preponderance of Leptothrix flora.

Recently Patocka and Reynes[6] have described a new anaerobic species of *Leptotrichia vaginalis.* They state that the particular morphology of this species places it in the genus *Lepotrichia Trevisan* but that it differs from both *L. innominata* and *L. tenuis.*

It is the purpose of this presentation to describe a filamentous strain of the bacillus of Döderlein found in the vaginas of pregnant women and identify it with the Leptotrichia (Leptothrix) of the earlier workers.

Materials and Methods

Wet-mount preparations of the vaginal discharges of 500 consecutive Negro and 200 white prenatal patients were examined microscopically for the presence of filamentous organisms and fungi. Those cases showing a profusion of the former were used to study the clinical manifestations and the various characteristics and properties of the bacterium.

Different media[7, 8] were inoculated for the isolation and maintenance of the organism but the hormone broth with a pH 4 and pH 5 and the glucose heart-infusion agar were most satisfactory. All cultures were incubated under increased carbon dioxide tension (10 per cent) at 37° C. Following the isolation of the filamentous bacterium from 11 Negro patients, its biochemic properties were studied and compared to those of a known strain of *Lactobacillus acidophilus* and 19 strains of the typical bacillus of Döderlein. Standard laboratory methods and procedures were employed.

To determine the period of survival of the organism in vivo the positive patients were re-examined after a period of one to three years.

Results

Incidence.—In the series of 500 Negro patients examined, 15.2 per cent showed this strain. Thirty-six, or 7.2 per cent, of the 500 patients harbored them to the extent of a plus 1 to a plus 2 reading and forty, or 8 per cent, had a plus 4 estimate. However, *only one of the 200 white pregnant women examined revealed this bacterial strain.* Also interesting was the high incidence of Candida infection (45 per cent) in patients showing maximum numbers (plus 4) of the bacteria.

Morphology.—In the unstained, freshly prepared wet smears, these filamentous organisms presented a whorled and tangled appearance. The skeins were made up of numerous flexible, filiform organisms individually composed of nonmotile rods. Wet mounts and stained smears showed these filaments with large numbers of squamous epithelial cells and free nuclei, with an occasional leukocyte, gram-positive cocci, or gram-negative rods and at times a few yeastlike cells and the pseudo-mycelia of Candida.

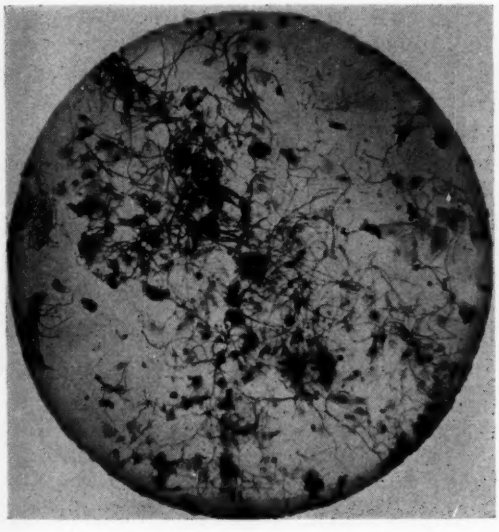

Fig. 1.

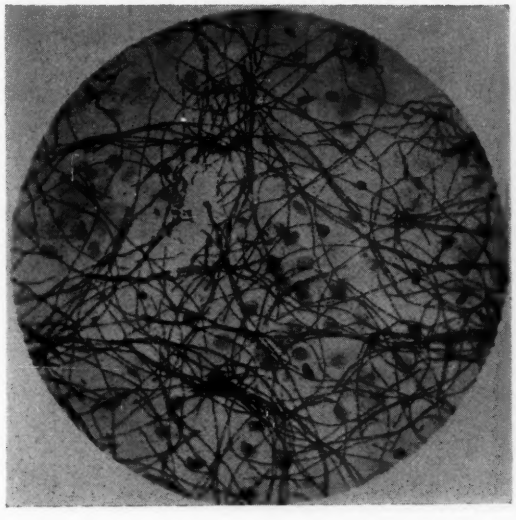

Fig. 2.

Fig 1.—Vaginal smear showing the filamentous strain of the bacillus of Döderlein. (Gram-stain preparation.) (×100.)

Fig. 2.—Methylene blue preparation showing the whorled and tangled appearance of the organism. Note the long, flexible, curving strands and epithelial cells. (×400.)

In the stained preparations the rods varied in length from 3 microns to 30 microns by 0.8 micron in width. They formed numerous long, delicate curves frequently curving upon themselves but rarely at right angles. The strands varied in length from 18 microns to 441 microns with an average of 38 microns (Figs. 1, 2, and 3). The bacterium was gram-positive and non-acid fast with a finely granular cytoplasm. With certain stains (Wright's hematoxylin and eosin) vacuolization was noted along the central longitudinal axis (Fig. 4). It possessed no spores or capsule and no volutin or glycogen granules were demonstrable.

Clinical Characteristics.—Of the 500 Negro patients examined there were 40 whose discharges showed a preponderance of this bacterium and 12 of these patients presented vaginal findings that could be attributed to this organism.

On questioning, the patients volunteered the information that they were conscious of a white discharge varying from slight to moderate in amount. An occasional patient complained of local itching and not infrequently of a burning sensation over the introital area following micturition.

Speculum examination revealed a moderate amount of discharge, moderately thin in consistency, of a mucoid nature, and of an even or speckled white color. The relative proportions of the constituents of the discharge were dependent upon the secretive activity of the cervix, number of bacterial filaments, and the amount of epithelial desquamation from the vaginal mucosa.

Inspection of the vagina showed a slight, diffuse erythema of the vaginal mucosa, but the characteristic finding was the numerous discrete, pin-head sized white areas scattered over the anterior third of the vagina. At times the introitus was involved and not infrequently the white flecks were seen over the posterior vagina and cervix. Microscopically these areas were colonies of strands of bacilli—a tangled mass of organisms with epithelial cells caught in the interstices of the filamentous bacteria.

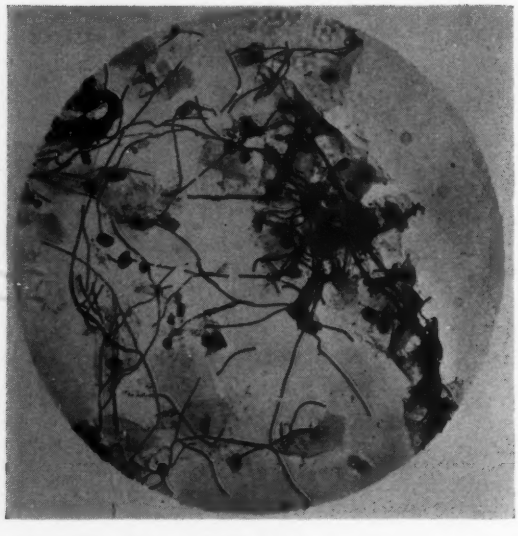

Fig. 3.

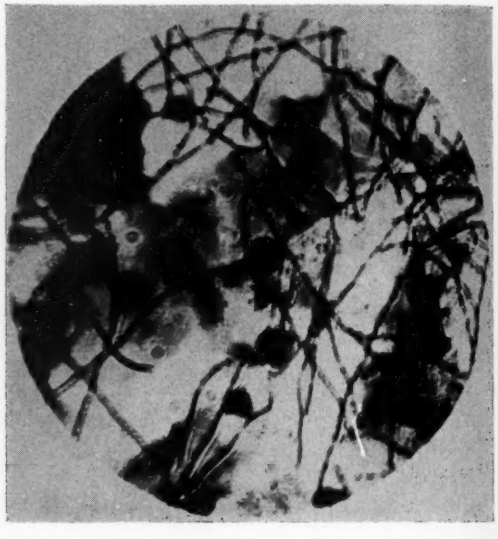

Fig. 4.

Fig. 3.—Showing the frequent association of this Lactobacillus with Candida. Note difference in size and characteristic branching and budding of the latter organism. (×400.)
Fig. 4.—Wright's stain preparation showing central vacuolization and beading. (×900.)

In contrast to the tenacious plaques of Candida, these white areas were lightly adherent to the vaginal mucosa. In a few instances, upon removal of these specks, there presented an area of ulceration. With the aid of a hand lens, the ulcer was observed to be superficial and irregular in outline with a congested base and built-up edges. This was seen more frequently when the bacterial colonies were associated with a Candida infection. In three patients the superficial ulcerations were diffused over the cervix and posterolateral vaginal walls.

In the 12 typical cases, direct determinations of the pH of the midvaginal mucosa were made by the glass electrode method with a Beckman pH meter and the range of pH varied between 3.6 and 4.7. The higher degrees of acidity were read within the characteristic white-flecked masses. Here pH recordings of 3.6 to 4.2 were obtained.

Survival of the Strain.—The presence of this bacterium persisted in a high percentage of the observed cases and appeared to exist regardless of the pregnant or nonpregnant state of the individual. Of the 37 of the 76 patients examined after one year, fifteen, or 40.5 per cent, were found positive. Several of these patients were re-examined on various occasions and the bacterial strain was present after a period of two to three years.

Cultural Characteristics and Biochemic Reactions.—The organism was isolated in pure form from 11 Negro women and typical Döderlein bacilli were cultured from 19 white women. All of the 30 cultures and that of *Lactobacillus acidophilus* produced long forms of the organism at a low pH of 3 and 4 resembling those from the discharges of the Negro patients and short forms at pH6 resembling those from the discharges of the white patients.

The cultural behavior and biochemic properties of the three groups were similar or interlocked sufficiently so that differentiation into species was not possible.

Comment

Filamentous bacterium has been described whose morphology is identified with the reported descriptions of Leptothrix and Leptotrichia of earlier workers.[1-5, 9] Furthermore, it is similar to Type C of three morphologic types of Döderlein's bacillus recognized by Cruickshank[10] which he describes as a streptobacillus growing in long chains of slender, even-sized bacilli and forming whorled masses.

The cultural characteristics and biochemic properties of the bacillus classify it as a member of the Lactobacillus group of organisms and in particular, *L. acidophilus.*[11-18] However, it differs from the organism reported by Patocka and Reynes.[6] The biochemic properties of the anaerobic *Leptotrichia vaginalis,* as set forth in their paper, place it in the genus Fusobacterium.[19-21] Therefore, the bacterium of this present study appears to be a variant of the bacillus of Döderlein, showing its characteristic filamentous form at a low pH of 3 and 4.

Although this strain is found frequently in association with a Candida infection, it is capable of producing a characteristic vaginal picture in a small percentage of the patients harboring the bacilli in profusion. However, the patients usually are asymptomatic, notwithstanding the observed areas of superficial ulcerations of the vagina.

Summary

In 76, or 15.2 per cent, of vaginal discharges from 500 pregnant Negro women examined, a filamentous strain of the bacillus of Döderlein was found. In forty patients, or 8 per cent, it occurred in maximum numbers and produced in twelve patients (30 per cent) the following vaginal picture.

A diffuse mild erythema was observed of the introital and vaginal mucosa upon the surface of which were scattered numerous discrete, pin-head sized white areas. These lightly adherent flecks were, microscopically, colonies of tangled bacterial filaments and epithelial cells. Superficial ulcers of the mucosa were beneath some of these masses, usually in association with a Candida infection.

However, of 200 pregnant white patients examined, this filamentous strain was found in only one individual.

The strain survived in the same patients for periods of one to three years.

The morphology of the bacillus was similar to the descriptions of that of Leptotrichia (Leptothrix) reported in the literature and was identified with the Lactobacillus group of organisms, especially *L. acidophilus,* in its microaerophilic characteristic and biochemic properties.

The authors are indebted to Drs. Lewis C. Scheffey, Thaddeus L. Montgomery, and Carl J. Bucher for the facilities of their departments and continuous interest in this work.

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AN EVALUATION OF VARIOUS METHODS OF VAGINAL ASEPSIS*

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THE purpose of this study is to evaluate the comparative effectiveness of a representative agent of each major family of antibacterials currently used in the vaginal preparation of the patient for gynecologic surgery. The primary impetus for this study stemmed from the appreciable consumption of nurses' time, during a period when the supply of nurses is critical, in carrying out the generation-old custom in this community of administration of bichloride of mercury douches in the preparation of gynecologic surgical patients. It is believed that with the development of antibacterial and antibiotic agents, in recent years, a more effective and less time-consuming method of vaginal preparation might be found.

Materials and Methods Used

A total of 325 unselected private patients admitted to St. Mary's Hospital for gynecologic surgery in the first half of 1951 were used for comparative evaluation.

Vaginal cultures were obtained from every patient admitted for gynecologic surgery before any type of medication was given. Preoperative cultures were obtained just before the patient was sent to the operating room. Postoperative cultures were taken on the fourth postoperative day in the majority of patients remaining in the hospital for that length of time. The cultures were obtained by using an ordinary cotton swab enclosed in a paper sheath beveled at one end. The sheath with the enclosed swab was inserted into the posterior fornix. The swab was thrust out of the end of the sheath, twisted to pick up the culture specimen, and withdrawn into the sheath. The whole device was then withdrawn from the vagina, the swab being protected from contamination by the surrounding sheath. The swabs were quantitatively cultured by swirling each swab ten times in a tube containing 12 c.c. of melted triptose agar culture medium. The inoculant was then poured onto a Petri plate and incubated for 24 hours at 37.5° C. Then the number of colonies was counted. The culture was quantitative only. It was felt that the cost of qualitative evaluation of the number of cultures involved would be too far out of proportion to the additional information derived therefrom to warrant its inclusion.

The cultures were reported as the number of colonies counted. The maximum reportable number being 10,000 because of the coalescence of colonies when the number of colonies was great.

In this study six groups of 50 patients each received bichloride of mercury douches, Merthiolate and glycerin instillations, Ceepryn vaginal suppositories, penicillin vaginal suppositories, penicillin and streptomycin vaginal suppositories, and no vaginal asepsis, respectively. One group of 25 patients received

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Furacin vaginal suppositories. The preparations used in this study were chosen because they are the members of their particular chemical families most suitable to clinical use; i.e., effective antibacterial agents, of low toxicity, easily administered, and readily available. A clinical evaluation of the antibacterial activity of these products in the vagina was considered advisable for comparison.

All vaginal preparations were administered in the afternoon before surgery and at 5 A.M. on the day of surgery. Patients receiving suppositories were given only one as indicated. Patients receiving Merthiolate and glycerin were given one ounce of the mixture instilled into the vagina with a catheter at each administration. The bichloride of mercury douches were in 1:3,000 dilution. Two quarts of the solution were used in the afternoon and again the following morning.

Review of Related Literature

Inorganic mercurial salts, especially bichloride of mercury, have been used for over 60 years as antiseptic compounds, but are not now considered to be as effective as originally believed. Early investigators misinterpreted their bacteriostatic powers as being bactericidal.[1, 2]

Organic mercurial salts, represented in this study by Merthiolate, are bactericidal to common pathogenic organisms on brief exposure[3, 4, 5] and have been used in the female genital tract with favorable results.[6, 7]

The quaternary ammonium compounds have a powerful antibacterial action.[8] Ceepryn brand of cetylpyridium chloride has been used effectively in the bronchial tree,[9] in preoperative antisepsis of the skin,[10] and in the vagina.[11]

Furacin brand of nitrofurazone N.N.R., a member of the furan group of compounds, has been shown to be an effective bactericide and has been used topically in superficial wounds and lower urinary tract infections with satisfaction.[12, 13]

Penicillin has been used in the form of vaginal suppositories with gratifying results by many authors.[14-20]

Streptomycin has also been used in the female genital tract with encouraging results.[21]

Laboratory and Clinical Results

The operative procedures for which the patients in this study were prepared are summarized in Table I.

TABLE I. OPERATIVE PROCEDURES

AGENT USED	TOTAL CASES	MAJOR CASES	MINOR CASES
No vaginal medication	50	29	21
Furacin suppositories	25	9	16
Bichloride of mercury douches	50	29	21
Merthiolate and glycerin instillations	50	17	33
Ceepryn vaginal suppositories	50	21	29
Penicillin vaginal suppositories	50	27	23
Penicillin and streptomycin suppositories	50	29	21

The preoperative cultures taken after the various methods of preoperative vaginal asepsis are presented in Table II.

The postoperative cultures showed uniformly high bacterial counts on the fourth postoperative day regardless of preoperative medication or preoperative cultures, except in those who received vaginal medication postoperatively. The uniformity of high postoperative culture counts is shown by the

comparison of the results in the 171 postoperative cultures taken from all patients not receiving postoperative vaginal medication, with the results in 34 patients who had low preoperative cultures from the penicillin and penicillin and streptomycin groups who received no postoperative medication.

TABLE II. CULTURES AFTER PREOPERATIVE PREPARATION

AGENT USED	NEGATIVE CULTURES (PER CENT)	LESS THAN ADMISSION CULTURES (PER CENT)	GREATER THAN ADMISSION CULTURES (PER CENT)
No vaginal medication	28	24	48
Furacin suppositories	32	24	44
Bichloride of mercury douches	56	16	28
Merthiolate and glycerin instillations	58	8	34
Ceepryn vaginal suppositories	62	12	26
Penicillin vaginal suppositories	80	10	10
Penicillin and streptomycin suppositories	84	8	8

However, 23 patients in this study received either penicillin or penicillin and streptomycin suppositories postoperatively, and had either negative postoperative cultures or relatively low postoperative culture counts. For example, the two patients receiving penicillin and streptomycin suppositories postoperatively, whose postoperative culture was not less than the admission culture, had postoperative culture counts of 164 and 72 colonies, respectively, while the 14 patients in the same group who received no postoperative vaginal medication and whose postoperative cultures were greater than their admission cultures had an average colony count of 9,650. The results of the postoperative cultures are summarized in Table III.

TABLE III. SUMMARY OF POSTOPERATIVE CULTURES

	TOTAL CASES NO.	NEGATIVE CULTURES (PER CENT)	LESS THAN ADMISSION CULTURES (PER CENT)	GREATER THAN ADMISSION CULTURES (PER CENT)
No postoperative medication, all cases	171	15	13	72
No postoperative medication, penicillin and streptomycin and penicillin groups	34	18	9	73
Postoperative medication with penicillin and streptomycin or penicillin suppositories	23	43	35	22

No patient in the entire series showed any irritation from or reaction to any of the agents used.

Postoperative morbidity in the groups was as follows:

Four patients who had no preoperative vaginal asepsis had morbid postoperative courses. One had a wound infection after an abdominal hysterectomy, one had a hematoma following a vaginal plastic procedure. One patient had an episode of acute endometritis following a curettage. The fourth patient became febrile after a transfusion reaction.

No patient in the Furacin group had a morbid course.

Five patients in the bichloride of mercury group were morbid. Two of these cases were directly attributed to hematoma formation following vaginal

plastic procedures. One patient developed a wound abscess after total hysterectomy. There was no obvious cause for the morbidity in the other two cases, one abdominal hysterectomy and one vaginal hysterectomy.

Of the patients receiving Merthiolate and glycerin instillations, there were two who were morbid. One had a wound infection following total abdominal hysterectomy, the other following a major vaginal procedure.

There was one morbid postoperative course in the Ceepryn group in a patient who had a radical abdominal hysterectomy for carcinoma of the cervix.

Three patients of the penicillin vaginal suppository group had morbid postoperative courses. One developed a wound infection after a total abdominal hysterectomy and bilateral salpingo-oophorectomy for pelvic inflammatory disease. One patient developed a bowel obstruction and had an evisceration on the sixth postoperative day. The third patient ran a febrile course following conservative surgical therapy for endometriosis.

One patient in the penicillin and streptomycin group had a morbid postoperative course. In this case both the preoperative and the postoperative vaginal cultures were negative. It was not believed that the morbidity was due to sepsis of vaginal origin.

The low incidence of morbidity for the 325 cases included in the study, 16 cases, or an incidence of about 5 per cent, is explained by the fact that only about one-half (161) of the operative procedures were considered as major procedures. Approximately an equal number (164) were minor procedures and uncommonly associated with morbidity.

The morbidity separated into the major and minor groups shows an incidence of about 10 per cent in the major group and less than 1 per cent in the minor group.

The size of each of the groups considered is too small for postoperative morbidity to be of any comparative significance, but even in this small series it is evident that basic surgical technique is of primary importance in the incidence of postoperative morbidity.

Summary

Three hundred twenty-five unselected gynecologic patients were divided into seven groups and were prepared for surgery by the use of bichloride of mercury douches, Merthiolate and glycerin vaginal instillations, Furacin vaginal suppositories, Ceepryn vaginal suppositories, penicillin vaginal suppositories, penicillin and streptomycin vaginal suppositories, and no vaginal medication, respectively.

Quantitative vaginal cultures were taken on admission and immediately preoperatively on all patients. Postoperative cultures were taken on the fourth postoperative day on the majority of patients.

Quantitative cultures showed penicillin vaginal suppositories and penicillin and streptomycin vaginal suppositories to be definitely more effective than the other antibacterial agents used in this series in the preoperative vaginal preparation of the gynecologic patient.

Postoperative use of penicillin vaginal suppositories and penicillin and streptomycin vaginal suppositories maintained a nearly sterile field for healing in the majority of cases.

Conclusions

Penicillin and streptomycin vaginal suppositories and penicillin vaginal suppositories were found to be the most effective antibacterial agents used in this study in the preoperative vaginal preparation of gynecologic patients.

The postoperative use of penicillin and streptomycin vaginal suppositories and penicillin vaginal suppositories maintained a relatively sterile field to promote postoperative healing.

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THE BALANCED MIXTURE FOR TERMINAL ANESTHESIA IN THE PARTURIENT

Preliminary Report

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THE use of the "balanced mixture" for anesthesia in general surgery, following a clinical trial in 10,000 cases, has already been reported.[1] It was decided to evaluate its usefulness as terminal anesthesia in the parturient.

The balanced mixture is a synergistic anesthesia combination consisting of approximately half the anesthetic dose of nitrous oxide (45 per cent) and cyclopropane (10 per cent) administered with 45 per cent oxygen in a semiclosed absorption system, in conjunction with amnesic sedation or a single hypnotic dose of an intravenous barbiturate.

The rational pursuant to its use in obstetrics was to have available a general anesthesia technique in the delivery room which would:

1. Serve as a nondepressing general anesthesia alternative for the excessively sedated patient who refused saddle or caudal block.
2. Diminish the incidence of vomiting in the parturient during the induction and maintenance stages of anesthesia.
3. Be simple to administer for inexperienced or occasional anesthetists such as residents and interns.
4. Not unduly depress the fetus.
5. Maintain the patient in a consistent light Plane I anesthesia without the "seesaw" imminence of sudden light and sudden deep anesthesia.
6. Not increase the incidence of postpartum hemorrhage.

Technique

The balanced mixture is utilized as a terminal general anesthesia to provide unconsciousness during the time of actual delivery and for any postpartum repair.

Two types of parturients will enter the delivery room. One type will be sedated with one or more of such drugs as Demerol, scopolamine, Sigmodal, paraldehyde, Seconal, Nembutal, etc. The other type will have had no sedation. The technique differs slightly for each of the two types.

The Sedated Patient.—

A rubber anesthesia mask is placed on the patient's face, the exhalation valve always remaining open (Fig. 1). The rubber breathing bag is filled with nitrous oxide and the anesthesia flowmeters are immediately set to deliver:

Oxygen	1,500 c.c. per minute (45 per cent)
Nitrous oxide	1,000 c.c. per minute (45 per cent)
Cyclopropane	300 c.c. per minute (10 per cent)

The percentage figures relating to the gases are, of course, approximate and are by no means exactly what exists in the alveoli or in the blood stream. This involves so many variables that exact figures are difficult to obtain. It would appear that the 1,500 c.c. of oxygen would be more than 45 per cent since 1,000 c.c. of nitrous oxide are also labeled 45 per cent. The reason for this apparent discrepancy is the minute-to-minute utilization of oxygen, whereas the nitrous oxide is inert, reaches an equilibrium with the circulating blood, and retains a comparatively constant concentration. Since oxygen is constantly consumed an additional 500 c.c. per minute is required to maintain an approximately equal percentage with the nitrous oxide.

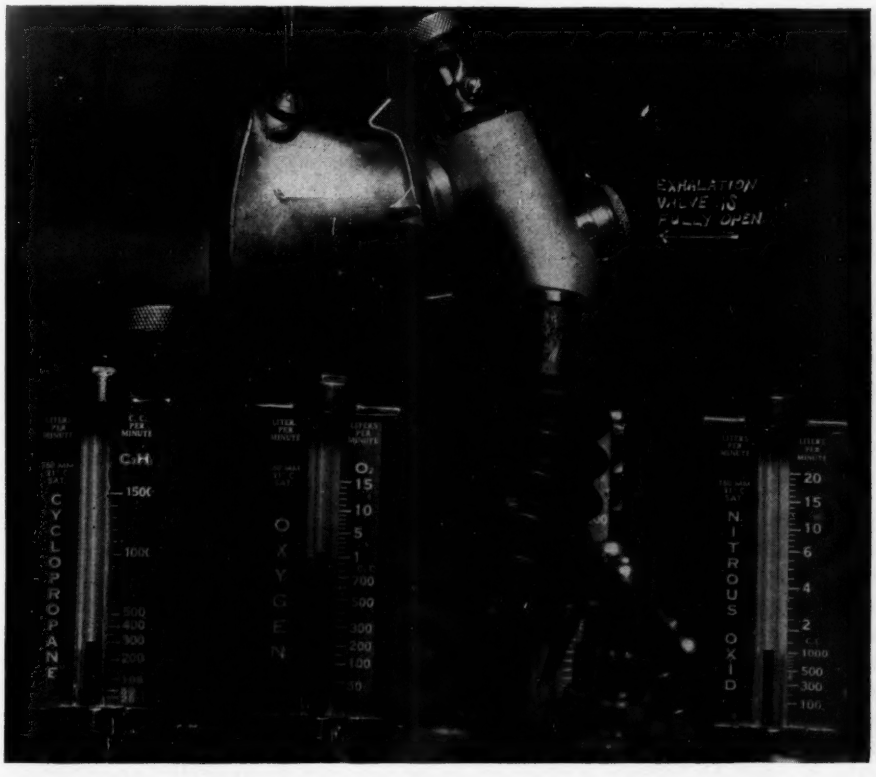

Fig. 1.—Flowmeter settings for the balanced mixture. Cyclopropane flows at 300 c.c. per minute, oxygen 1,500 c.c., and nitrous oxide 1,000 c.c. per minute. The exhalation valve is open fully at all times to permit the escape of carbon dioxide along with the excess gases.

This large volume flow of gases prevents the accumulation and retention of carbon dioxide as seen in closed system anesthesias by permitting a portion of each exhalation to be blown out of the exhalation valve into the operating room. It furthermore prevents the accumulation of cyclopropane, thus obviating a gradual deepening of the anesthesia. Upon inhalation the valve closes and prevents the entrance of room air. Fresh soda lime should be used in the system to eliminate those traces of carbon dioxide which may not be completely eliminated via the exhalation valve.

Within two minutes of breathing this mixture the patient is unconscious. Most patients are anesthetized in less than two minutes. The patient will remain in Plane I anesthesia and will not descend deeper than this plane regardless of how many hours she breathes the gases. As the fetal head is being delivered, the nitrous oxide and cyclopropane should be temporarily turned off,

the bag flushed out, and 100 per cent oxygen administered continuously at a high flow of 10 L. or more per minute until the umbilical cord is clamped. The cord, if pulsating, should be permitted to continue to pulsate for a minute or two so that the oxygen which the mother is breathing will benefit the child. This step is highly important.

After the cord is clamped the breathing bag is again squeezed until it is emptied of oxygen. It is refilled with nitrous oxide and the flowmeters are once more set at 1,000 c.c. for nitrous oxide, 1,500 c.c. for oxygen, and 300 c.c. for cyclopropane. It is remarkable to observe how smoothly patients drift into consciousness when the 100 per cent oxygen is administered as the head is delivered, and lapse into unconsciousness with the re-establishment of the balanced mixture for repair of episiotomy.

The Unsedated Patient.—

The parturient entering the delivery room who has received no sedation whatsoever during labor will react to the balanced mixture differently from the sedated patient. She may vomit during the induction stage, she may struggle violently during the excitement stage, or she may remain in the struggling excitement stage and never quite reach Plane I of the surgical stage, or she may finally reach Plane I after a prolonged period of breathing the mixture. It is for these reasons that some intravenous hypnotic should be administered to the unsedated parturient immediately before the mask is placed on her face. We prefer intravenous Nembutal in the amount of 2 c.c. (100 mg. or 1½ grains) although Evipal, Pentothal, Surital, or intravenous Demerol, 50 to 100 mg., may be used equally effectively. If Evipal, Pentothal, or Surital is used, the dose should not put the patient completely to sleep, but make her only sleepy or amnesic. This small dosage range will of course avoid undue fetal respiratory depression.

Comment

In this series the Heidbrink machine was used. Most machines, however, may be utilized for this anesthesia. The percentages of both nitrous oxide and cyclopropane used in the balanced mixture are in reality about half of what it would require for complete anesthesia if either of the gases were used alone. Thus, it would require at least 80 per cent or more of nitrous oxide to produce anesthesia if it were used only with oxygen. It requires from 15 to 20 per cent when cyclopropane is used alone. Yet a combination of the two gases at half their anesthesia range will produce and maintain light anesthesia indefinitely, providing the patient has been amnesically sedated or an intravenous barbiturate is used to induce a state of hypnosis, not necessarily anesthesia. This implies that, regardless of the number of hours the operation progresses, no additional sedation or intermittent doses of barbiturates will be required.*

In an attempt to explain this phenomenon the work of Barbour[2] may be pertinent. Barbour demonstrated that when barbiturates or morphine are injected into animals a shift occurs in the brain water balance. The cerebral cortex loses water which is taken up by the medulla. As the effect of the barbiturate diminishes and a return to normal cerebration supervenes, the medulla gives up the water and the cerebral cortex rehydrates. Prout[3] expressed the view that the inhalation of the nitrous oxide and cycloprapane in the balanced mixture concentration is perhaps sufficient to maintain the water shift so that consciousness would not return until the gases were discontinued.

This explanation is, of course, theoretical, and is offered only as an attempt to explain the consistently predictable action of the balanced mixture when

*When the balanced mixture is used for general surgery the attainment of satisfactory abdominal relaxation is precluded due to the lightness of the anesthesia plane. Intermittent injections of curare are therefore necessary to produce relaxation.

used in conjunction with amnesic sedation or an intravenous barbiturate hypnotic induction, and its bizarre unpredictability when amnesics or hypnotics are not used.

Results

1. In the 100 cases upon which this preliminary report is based there were no maternal deaths.

2. There was one infant death in the series. The mother neglected to report that the membranes had been ruptured for eight days prior to hospital admission, there was doubt about the infant prior to delivery, and at delivery, which was a midforceps application, the child was bathed in and had aspirated meconium, there being no heartbeat detectable at any time from the moment of delivery.

3. There were no patients who vomited during either the induction or maintenance phase of anesthesia. Fifteen per cent of the mothers vomited after they had fully awakened and were in control of their pharyngeal and swallowing reflexes. This observation has been previously reported in the 10,000 case surgical series where over 200 patients with histories of having eaten within 4 hours prior to emergency surgery for fractures, tendon repairs, etc., were anesthetized with the balanced mixture. None of these patients vomited during induction or maintenance. All of them did vomit after they were awake and in full control of their reflexes, thus diminishing the danger of aspiration of vomitus. We felt that the negation of vomiting seen with the balanced mixture was of considerable merit since so many of the obstetrical anesthesias in the United States are administered by inexperienced personnel.

This observation is in no way to be construed that vomiting may not occur. It may and no doubt will; and every parturient under any type of general anesthesia should be watched for this reaction, which is the largest single factor in maternal mortality from anesthesia.

There were two patients who vomited during the 100 per cent oxygen period prior to the clamping of the cord. This occurred when the patient was awakened because of the oxygen inhalation and in full control of her swallowing reflexes.

4. There were no cases of postpartum hemorrhage which exceeded 500 c.c. The amount of blood loss following the balanced mixture was no more than that seen following other types of general anesthesia.

5. A test analysis of the explosive range of the balanced mixture was made by Dr. George Thomas of the University of Pittsburgh and by Dr. Sylvan E. Foreman of the U. S. Industrial Chemical Corporation in Baltimore. Their findings indicated that the explosion hazard posed by the balanced mixture was no more than that encountered in using ether and cyclopropane or straight cyclopropane in a closed system. They stressed that all the usual precautions against explosions, such as grounding, should be observed.

6. The average breathing, crying, anesthesia, and sedation time factors were as follows: breathing time 15 seconds; crying time 29½ seconds; anesthesia time 6 minutes; sedation time 2¼ hours; operating time 20 minutes.

Breathing and Crying Time.—This was based upon a stop watch count which was begun the moment the entire child was out of the vagina. The longest breathing and crying time was 3 minutes in an infant whose mother had 3 grains (200 mg.) of Nembutal and 1/100 grain of scopolamine intravenously 45 minutes before delivery. Of the 100 cases in which all but 2 mothers were sedated with a barbiturate, Demerol and scopolamine, 57 infants breathed the very instant of delivery and, of these, 38 cried at the same instant. The remainder breathed in an average of 15 seconds and cried in an average of 29½ seconds. The percentage of spontaneous breathing times was therefore 57 per cent.

Anesthesia Time (6 minutes).—This was calculated from the moment the balanced mixture started until the time it was stopped and 100 per cent oxygen given prior to clamping the cord.

Sedation Time.—This averagel 2¼ hours and was based upon the time the last dose of sedation was given until the cord was clamped. Thus, if Demerol and scopolamine were given at 2 P.M. and the cord was clamped at 4:15 P.M., the sedation time would be 2¼ hours.

Operating Time.—This averaged 20 minutes and was based upon the time the balanced mixture was started until the operation itself (delivery, episiotomy, repair, etc.) was completed and the anesthesia mask permanently removed. The 100 per cent oxygen period was not deducted from this over-all figure.

Summary

A synergistic anesthesia combination called the balanced mixture was evaluated for obstetrical use and found to possess encouraging possibilities.

The balanced mixture was defined as a synergistic anesthesia combination consisting of approximately half the anesthetic dose of nitrous oxide (45 per cent) and cyclopropane (10 per cent) administered with 45 per cent oxygen in a semiclosed absorption system, in conjunction with amnesic sedation or a single, partially hypnotic dose of an intravenous barbiturate.

The technique and rationale for its administration were detailed. The results indicated that the balanced mixture was not overly depressing to the fetus, that it was simple and comparatively safe for obstetrical interns and residents to administer, and that maternal vomiting during anesthesia was decidedly diminished, thus helping to obviate one of the major causes of maternal mortality.

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A TEST FOR LACTATION SUCCESS

A Preliminary Report

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THE object of this study was to find a simple laboratory test which could be used to predict a nursing mother's ability to produce an adequate supply of milk. Waller's report[1] indicated that among women in whom lactation was well established the increase in the fat content of milk during a single nursing was due to a draught or let-down reflex. Newton and Newton[2] showed success in early lactation to be related to the function of this reflex. When proper let-down occurs, fat-rich milk is expelled from the alveoli of the breast into the larger ducts to become available at the nipple. With normal function, later samples of milk should contain considerably more fat, while with subnormal function little or no increase in the fat content should occur. The difference in the fat content of the milk before and after nursing might therefore be used in early lactation to appraise the function of the let-down reflex and to predict the success of lactation.

Material and Methods

A group of 25 mothers in the Maternity Ward of the Hospital of the University of Pennsylvania were used in this study. These patients were selected inasmuch as they had experienced uncomplicated antepartum courses, spontaneous or simple instrumental deliveries, and normal postpartum courses. The breasts and nipples of all were grossly normal and the babies were mature and healthy. At the time of this study, the breast feeding practice in use at the hospital consisted of scheduled feedings which permitted liberal sucking. Mothers were strongly urged to breast feed their babies. The babies were brought to the mothers every 4 hours, for 30 to 45 minutes, starting 24 hours after birth. For the first few feedings the time of sucking was somewhat limited and thereafter it was permitted for the whole time during which the baby was with the mother.

Tests for milk fat were performed in all cases on the fourth postpartum day, i.e., at an average of 98 hours (range 80 to 110 hours) after delivery. A specimen of milk (3 to 5 c.c.) was obtained from one breast by means of an electric breast pump at the regular nursing time just before the baby was brought in. The baby was then allowed to nurse until he was satisfied or refused to continue, usually 30 to 45 minutes, starting on the side from which the specimen had been taken. As soon as possible thereafter, 3 to 5 c.c. of milk were taken as before from the same breast.

The babies were weighed before and after all feedings on the fourth postpartum day, including the test feeding, and the average amount of milk obtained at a fourth-day feeding was computed. In addition, the mothers were

questioned concerning symptoms suggestive of function of the let-down reflex, both at previous feedings and during the test feeding. These symptoms were: (1) uterine pain during nursing, (2) dripping of milk before the baby was put to the breast, (3) dripping of milk from the opposite breast, (4) cessation of nipple pain during nursing. The significance of these symptoms has been discussed in a previous publication.[2]

The specimens of milk which were obtained before and after nursing were analyzed for fat by a modification of the Leffmann-Beam method.[3] After the sample had been mixed, 2.5 c.c. were placed in a special tube.* One c.c. of a mixture of equal parts of amyl alcohol and concentrated hydrochloric acid was added and the tube was filled with 75 per cent sulfuric acid to just above the graduated marks on the narrow neck. The tube was then centrifuged for five minutes at approximately 1,500 r.p.m. and the percentage of fat in the sample was read off from the graduated scale. The resultant figure was then doubled since 2.5 c.c. instead of 5 c.c. (as originally described) were used. Readings were made with confidence to 0.1 per cent (0.2 per cent after correction) and repeated determinations on the same sample of milk agreed satisfactorily.

Results

The difference in the fat content of the two specimens in successful and unsuccessful breast feeders is seen in Tables I and II. The mean initial fat content of the milk was approximately the same in the two groups: 2.8 per cent in the successful and 2.9 per cent in the unsuccessful group. The difference in the mean increase, however, was quite definite: 2.0 per cent in the successful and only 0.2 per cent in the unsuccessful group. This difference is statistically significant (p less than 0.05). Of the 15 successful breast feeders, only 3 gave an increase of under 1 per cent. Of those who were unsuccessful, 10 in number, only 2 gave an increase of over 1 per cent.

TABLE I. DIFFERENCES IN FAT CONTENT OF HUMAN MILK IN 15 SUCCESSFUL* BREAST FEEDERS

	FAT CONTENT OF MILK		
	BEFORE NURSING %	AFTER NURSING %	DIFFERENCE %
	3.2	11.0	7.8
	3.6	9.0	5.4
	2.2	4.2	2.0
	3.2	5.0	1.8
	2.2	4.0	1.8
	1.8	3.6	1.8
	0.4	2.2	1.8
	3.0	4.8	1.8
	6.0	7.5	1.5
	2.0	3.4	1.4
	4.0	5.2	1.2
	2.8	4.0	1.2
	2.8	3.2	0.4
	2.4	2.6	0.2
	2.4	2.6	0.2
Mean	2.8	4.9	2.0

*A successful breast feeder was defined as one whose baby was fed entirely by breast on the fifth postpartum day.

The increase in fat content showed a positive correlation with the amount of milk taken by the baby at the test feeding and a greater but not significant positive correlation with the average amount of milk given at a fourth-day

*Manufactured by the A. H. Thomas Co., Philadelphia, Pa.

feeding. The successful mothers gave a mean of 76 Gm. of milk during an average fourth-day feeding while the unsuccessful mothers gave a mean of only 34 Gm. The difference between the two groups is highly significant (p less than 0.01).

TABLE II. DIFFERENCES IN FAT CONTENT OF HUMAN MILK IN 10 UNSUCCESSFUL* BREAST FEEDERS

	FAT CONTENT OF MILK		
	BEFORE NURSING %	AFTER NURSING %	DIFFERENCE %
	4.2	6.8	2.6
	1.2	2.4	1.2
	1.6	2.0	0.4
	1.6	2.0	0.4
	3.0	3.0	0.0
	3.0	3.0	0.0
	4.4	4.0	–0.4
	2.4	1.8	–0.6
	2.0	1.2	–0.8
	5.6	4.6	–1.0
Mean	2.9	3.1	0.2

*An unsuccessful breast feeder was one whose baby required a supplementary formula on the fifth postpartum day.

The relation between the let-down symptoms and the increase in fat content of the milk is seen in Table III. When the four symptoms of let-down were totaled they occurred more frequently in mothers who had an increase in fat of more than 1.3 per cent than in those who had an increase of less than 1.3 per cent. This difference was slight before the test nursing but significant (p less than 0.05) during the test nursing. Differences were most marked in "milk dripping before nursing" and in "milk dripping from opposite breast during nursing." The slight differences in the other two symptoms may be explained by the low over-all incidence of "uterine pain" on the fourth postpartum day and the relatively small number of cases in the "cessation of nipple pain" group.

TABLE III. INCREASE IN FAT CONTENT OF HUMAN MILK DURING NURSING AND LET-DOWN SYMPTOMS

	MOTHERS WITH SYMPTOMS PRESENT			
	BEFORE TEST NURSING		DURING TEST NURSING	
	FAT INCREASE MORE THAN 1.3%* (11 CASES)	FAT INCREASE LESS THAN 1.3% (14 CASES)	FAT INCREASE MORE THAN 1.3% (11 CASES)	FAT INCREASE LESS THAN 1.3% (14 CASES)
Uterine pain while nursing	64%	62%	18%	23%
Milk dripping while nursing	73%	46%	73%	23%
Milk dripping from opposite breast while nursing	91%	75%	100%	62%
Cessation of nipple pain while nursing	88%	100%	100%	100%
All symptoms†	78%	67%	71%	48%

*1.3 per cent represents the mean of all increases in fat content during nursing.

†Occasional symptoms were unclassifiable, e.g., some mothers stated that they had no nipple pain.

Comment

The fat difference test is the newest of several methods of judging the adequacy of lactation. No test is as good as the continued health and weight

gain of the baby. During early lactation, however, other tests are needed, among which are the clinical estimation of the baby's ability to take the breast and weighing before and after nursing. The former may be very helpful but is necessarily inexact. Test weighing (repeated rather than single) has been the most reliable guide to the adequacy of lactation up to the present. It is, however, a nuisance to the nursing staff and may upset the mother. Furthermore, both the caloric content of the human milk and the individual caloric requirement of the baby may vary. Measurement of the quantity ingested does not take such variations into account. The fat difference test is a valuable adjunct to other methods and it may permit a decisive opinion reasonably early in the breast feeding trial. It is simple and requires only 15 minutes to perform. Only one feeding need be disturbed for the test and the sample of milk required is so small that it does not appreciably lessen the quantity available to the baby.

This test can also be used as a measure of let-down reflex function. Previously this was evaluated by the presence or absence of symptoms of let-down and by measurement of the proportion of milk left in the breast after nursing by inducing artificial let-down by the injection of Pitocin (Pitocin percentage).[2] The disadvantage of using these symptoms is that they are subjective and are based upon abnormal sensations, such as pain. The determination of Pitocin percentage is difficult in the presence of severe engorgement, just when it is most needed. The fat difference test is not subjective, it is applicable to all mothers, and appears to give a reasonably good indication of let-down reflex function.

While the clinical value of this test is not proved, it seems to have definite promise. In many mothers, knowledge of their attitude toward breast feeding[4] and observation of their early attempts to lactate will indicate without further study the likelihood of success or failure. There are some whose attitudes are doubtful and in whom the onset of lactation is precarious and difficult. It would seem worth while in such individuals to perform the fat difference test on the third or fourth postpartum day in addition to test weighing. If the fat increase is less than 1 per cent the outlook is not good but the effort to breast feed should not be abandoned. All possible measures should be instituted to forestall lactation failure. Such measures include:

1. Sympathetic encouragement of the mother with a simple explanation of the physiological mechanisms that are involved.
2. Privacy during nursing.
3. Relief of nervous tension by giving mild sedatives throughout the day.
4. The assurance of relaxation and freedom from pain during nursing by giving mild analgesics or alcohol prior to nursing.
5. Provision for adequate sucking stimulation by allowing eight feedings or more a day, and by instructing the mother to empty her breasts manually after the baby has nursed.
6. Immediate attention to sore or damaged nipples.

These measures are particularly important at the present time when the postpartum stay in the hospital has become shorter and the mother has barely time to establish lactation before she is faced with the difficult physical and emotional transition from the hospital to the home. This test may enable the medical adviser to predict the success of continued breast feeding and to advise his patients prior to their discharge from the hospital. Further work is being done to substantiate the validity of the deductions that are based upon this study. Its promise justifies a preliminary report in the hope that its clinical value will be tested by others.

Summary

1. The fat content of human milk was determined before and after nursing on the fourth postpartum day in 25 mothers at the Hospital of the University of Pennsylvania.

2. A modification of the Leffmann-Beam method, employing 2.5 c.c. of milk, was used for determining fat.

3. Mothers who lactated successfully during their hospital stay showed a greater increase in the fat content of their milk than those who were unsuccessful.

4. Symptoms of function of the let-down reflex were present more frequently in those mothers who showed a greater increase in fat than in those who showed a smaller increase.

5. The clinical application of this test was discussed.

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RESIDUAL CARCINOMA IN THE VAGINAL CUFF AFTER RADICAL HYSTERECTOMY WITH BILATERAL PELVIC LYMPH NODE DISSECTION

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SUCCESSFUL surgical treatment of cancer is possible only if the maximun extent of the tumor can be identified or estimated. An intimate knowledge of the way a cancer behaves in a particular location is the best way of estimating the extent of a lesion. In cancer of the cervix this is of great importance. Its gross extension into the parametrium and regional nodes, upward into the corpus, and down into the vagina has a counterpart in its microscopic extension in the same directions. Much attention has been focused on the parametrium and regional node involvement. The extent of corpus involvement is of less importance because a total hysterectomy is the usual routine. It is our purpose to direct attention to the extension of tumor in the vaginal epithelium beyond the area of gross involvement. Even though one may take a generous vaginal cuff well outside the visible tumor, histologic section may show cancer extending to the cut edge. As early as 1896 Mackenrodt recognized the problem, pointing out the possibility of vaginal extension and the difficulty in recognizing it grossly.

Material

In a series of 300 radical operations for cancer of the cervix, this complication has been encountered seven times, all within the last three years. The cases are listed in Table I. The clinical extent of disease, according to the International Classification, was Stage I in two cases, Stage II in four, and Stage III in one. There was gross involvement of the vagina at the time of operation in five. The histologic classification was not significant since there were four in Grade II and three in Grade III. When the specimen is removed at operation the vaginal cuff invariably contracts, presenting a much shorter length than it appeared to have during the course of the operation. The widths recorded here were measured in the Pathology Laboratory some time after the removal of the specimen, after the vagina had contracted, and measured from 1.3 to 8.0 cm. In five cases the margin of free vagina beyond the tumor was 1.3 to 4.5 cm. In Case 2 there was slight gross thickening at the cut edge which was recognized at operation but not thought to be cancer. In Case 5 the margin was not recorded. Regional nodes were involved in three of seven cases.

Treatment

Five of the cases were treated by reoperation, either vaginal or abdominal, and the remaining vagina was excised. This was not done in one patient and she died of her disease in spite of palliative radiation given one year after her operation. The last patient was operated upon three months ago and is being

urged to return for further treatment. The interval between the two operations varied from 15 days to four months. In the original specimen the tumor was called invasive histologically at the cut edge in four patients, and cancer in situ in three. The specimen removed at the second operation showed an in situ lesion in two, an invasive lesion in one, and no tumor in two. One patient (Case 1) has died of cancer at two years and the remainder have no gross evidence of disease from four months to two years.

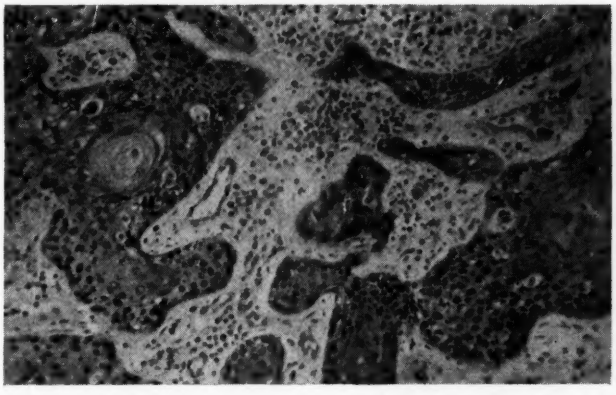

Fig. 1 (Case 3).—Invasive carcinoma in the distal vaginal cuff in specimen.

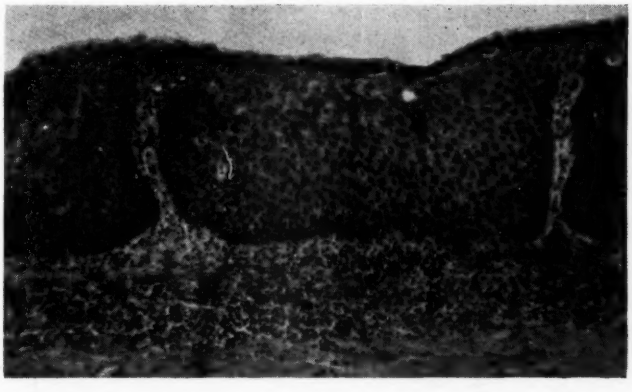

Fig. 2 (Case 3).—Carcinoma in situ in the vaginal remnant removed at a second operation.

Carcinoma in situ which is rarely detected on inspection may extend in the vaginal mucosa at least 4.5 cm. beyond the gross tumor. Invasive carcinoma has been found to extend at least half that far without being detected at operation or immediately afterward on gross inspection of the specimen. This is not the only area where tumor may be inadvertently left behind at operation, but it is an area where the mistake should be avoidable. Failure to recognize and treat persistent cancer left here may be associated with a fatal outcome. The vaginal extension in Case 1 was not treated promptly because of a complex situation, and she has died of her disease. When she was first seen in our clinic, there was a local recurrence in the pelvis following a total hysterectomy done for cancer of the cervix three years previously. A part of the bladder, one ureter, and the external and internal iliac veins on one side were removed along with most of the remaining vagina. Her postoperative course was stormy and, therefore, prompt reoperation on the vaginal extension found microscopically was not carried out. In retrospect, she should have been operated upon without delay.

TABLE I

CASE NO.	YEAR OF OPERATION	CLINICAL		HISTOLOGIC GRADE	WIDTH OF VAGINAL CUFF	MARGIN OF FREE VAGINA BEYOND GROSS TUMOR	INVOLVEMENT OF REGIONAL NODES	INTERVAL BETWEEN OPERATIONS	CHARACTER OF TUMOR AT CUT EDGE IN FIRST SPECIMEN	TUMOR IN SECOND SPECIMEN	FOLLOW-UP
		STAGE	INVOLVEMENT OF VAGINAL WALL								
1	1948	III	+	III	2 cm.	2 cm.	+	—	Invasive	—	Died of recurrence 2 years
2	1949	II	+	II	6.5 cm.	?	+	4 months	Invasive	Invasive	Ok at 18 months
3	1950	II	+	II	6 cm.	2.6 cm.	0	15 days	Invasive	In situ	Ok at 10 months
4	1950	I	0	II	1.3 cm.	1.3 cm.	0	15 days	In situ	Invasive	Ok at 5 months
	1950	II	+	III	8 cm.	—	0	2 months	Invasive	0	Ok at 6 months
6	1951	II	+	II	4.5 cm.	4.5 cm.	+	5 weeks	In situ	0	Ok at 2 months
7	1951	I	0	III	3 cm.	3 cm.	0	—	In situ	—	Died of intercurrent disease at 10 months

The result in Case 1 emphasized the danger of this complication. Ideally, a vaginal extension should be recognized before operation and removed at that time. This is not always possible, as this sort of extension may be recognizable only in the histologic section. Schiller's test is of definite value, but is not completely accurate because the vaginal wall frequently stains poorly and irregularly. The complication of unrecognized microscopic cancer has only recently been brought to our attention, and the cases reported here did not have a careful iodine test of the entire vaginal wall. Multiple biopsies of the vagina could be done to rule out such extension before operation, but they are not usually carried out. From now on, a careful iodine test should help in making the diagnosis before operation. We must use our clinical judgment also, knowing that the cancer may extend well beyond obvious tumor. The pathologist should be aware of the problem and should cut the resected margin of the specimen in a way that will ensure recognition if such extension exists. The routine use of the vaginal smear postoperatively offers additional protection. Residual tumor or a recurrence of malignancy in the mucosa may be readily recognized cytologically. An occasional patient will require reoperation, and the reoperation may cure a patient who otherwise would die of further disease.

Summary

An invasive or in situ cancer of the cervix may occasionally extend in an unrecognized form beyond the gross tumor and thus inadvertently be left behind. Such extension of cancer will be recognized only on histologic section and will necessitate a second operation. In the Vincent Memorial Hospital this complication has occurred seven times in 300 cases, or in 2 per cent. One patient died of recurrence without further therapy. Five patients have been reoperated upon and in three cancer was found in the material removed at the second operation. This complication can be dealt with effectively if the surgeon and the pathologist are both aware of its possible occurrence.

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SUSTAINED CONTRACTIONS OF THE GRAVID UTERUS DURING SPINAL ANESTHESIA

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THERE is little information in the literature concerning the powerful sustained uterine contractions that may develop under spinal anesthesia at cesarean section. The effects of spinal anesthesia on the pregnant uterus during laparotomy and during cesarean section have been studied by Malpas.[1] He states that the normal motor function of the central nervous system on the pregnant uterus is inhibitory and that such inhibition is a sustained action, and not an intermittent one; spinal anesthesia to the tenth dorsal segment paralyzes the motor connection between the spinal cord and the uterus, releases contractions, and heightens the reactivity of the myometrium to stimuli. We present four patients on whom cesarean section was performed, whose myometrial patterns should be of interest to all who use spinal anesthesia during cesarean section.

Material

Four multiparas, whose ages ranged from 27 to 37 years, were delivered by cesarean section under spinal anesthesia after premature labor had commenced spontaneously. There were three transverse presentations with a prolapse of the arm in each instance, and one frank breech presentation. The amniotic membranes had been ruptured spontaneously from one to 120 hours, the labor had been in progress from two to four hours.

Case 1.—J. M., No. A748, a 28-year-old gravida iii, para ii, had an uneventful antepartum course until the thirty-fifth week of gestation when labor began. During a sterile vaginal examination, the amniotic membranes were accidentally ruptured, the right arm of the baby and the umbilical cord prolapsed through a cervix that was 3.0 cm. dilated and 40 per cent effaced. The presentation was a right scapuloposterior. Immediate cesarean section was performed under spinal anesthesia using 50 mg. of 10 per cent Novocain. A powerful sustained pathologic contraction ring developed tightly around the baby as a crescentic lower uterine segment incision was made. Immediately a longitudinal corporeal incision was made in the uterus in order to deliver the four pound, 1 ounce baby that died nine hours later. The multiple uterine incisions resembled an inverted letter *T*. The postoperative course was characterized by very marked abdominal pain. Seventeen months later the patient was delivered of twins at the thirty-fifth week of gestation after the spontaneous onset of labor by a classical cesarean section. There was no apparent thinning in the multiple uterine scars of the previous operation.

Case 2.—R. M., No. 1203, was a 27-year-old gravida ii, para i, who had been delivered by cesarean section. The second pregnancy was uneventful until the thirty-sixth week when the membranes ruptured spontaneously and labor commenced. The presentation was a frank breech, right sacrum anterior; the cervix was 3.0 cm. dilated and 40 per cent effaced. A cesarean section was done under spinal anesthesia using 10 mg. of Pontocaine. When the transverse lower segment uterine incision was made, the uterus contracted powerfully around the baby and changed the presentation to a left scapuloanterior. In order to deliver the baby, a longitudinal uterine incision was made that almost reached the fundus of the uterus.

A 4 pound, 3 ounce female infant was delivered that cried as soon as she was born. The infant was discharged from the hospital in good condition. The mother's postoperative course was characterized by marked abdominal pain.

CASE 3.—D. H., No. A896, a 37-year-old gravida iii, para ii, who had been a patient in a psychiatric institution in 1949, refused to come into the hospital, at the thirty-sixth week of an uneventful antepartum course, when the amniotic membranes ruptured spontaneously. When labor began 120 hours later, the patient reported to the hospital. A sterile vaginal examination revealed that the cervix was 4.0 cm. dilated, 50 per cent effaced. The presentation of the baby was left scapuloposterior with a prolapse of the left arm. Tightly and powerfully the uterus contracted around the baby when the crescentic lower segment uterine incision was made. A longitudinal incision into the body of the uterus was now made in order to deliver the 4 pound, 3 ounce female infant. The baby was discharged in good condition from the hospital. The patient was discharged on the tenth postoperative day, after a morbid course as defined by the American College of Surgeons, and after experiencing very marked lower abdominal pain.

CASE 4.—M. G., No. A2653, a 35-year-old gravida iv, para i, had an uneventful antepartum course until the thirty-fifth week of gestation when the amniotic membranes ruptured spontaneously, and labor began. A sterile vaginal examination revealed that the cervix was 4.0 cm. dilated and 40 per cent effaced. The presentation of the baby was found to be left scapuloposterior with a prolapse of the left arm. A cesarean section was done under spinal anesthesia using 10 mg. of Pontocaine. A longitudinal uterine incision was made after the uterus had contracted powerfully around the baby as soon as the lower uterine segment transverse incision was made. A 4 pound, 14½ ounce female infant was delivered that made good progress and was discharged from the hospital in good condition. Except for marked abdominal pain for three days postoperatively, the patient's course was nonmorbid.

Comment

In the study of the four cases reported in this paper, we were impressed with the powerful, sustained uterine contractions that developed at cesarean section, under spinal anesthesia, when the lower segment uterine incision was made. Malpas[1] has given considerable study to the problem of the frequency of uterine contractions during pregnancy at laparotomy and during cesarean section, with the use of spinal anesthesia. Up to the twelfth week regular uterine contractions occur. After the sixteenth week, uterine contractions occur irregularly, and may not be elicited again until late in pregnancy, usually about the thirty-sixth week, when the spinal anesthesia effect reappears, and spontaneous contractions of the mass pattern are released. Slight pressure or a scratch may set up a linear contraction in the uterus; however, under local or general anesthesia equivalent trauma has no such equivalent effect.

MacIntosh[2] reported a case of placenta previa with no evidence of fetal distress prior to the administration of spinal anesthesia. However, fifty minutes later when the uterus was incised, the uterus was found to be tightly contracted around the baby that had died in the interim. He reported a second case where a twenty-minute delay after the administration of the spinal anesthesia almost resulted in a stillborn infant due to a sustained contraction of the uterus, and a resultant hypoxia.

In three cases from a series of more than two thousand, Lull and Hingson[3] attributed a late partial separation of the placenta, and one case of total separation of the placenta to release of the uterine contractile forces through the inhibitory nerve block from spinal and caudal anesthesia.

In the present study multiple uterine incisions were necessary to deliver the baby in each instance in the presence of premature labor, where the amniotic fluid had drained away from the spontaneous rupture of the membranes, and where the uterine contractile mechanism had been released by spinal anesthesia.

Summary

1. We have reported a syndrome composed of the following components: (a) premature labor; (b) ruptured membranes; (c) an abnormal presentation of the baby; (d) the release of the uterine contractile mechanism by spinal anesthesia.

2. The abdominal wall should not be traumatized after the administration of the spinal anesthesia for fear of releasing the uterine contractile mechanism.

3. Oxygen should be administered routinely to mothers receiving spinal anesthesia in order to lessen the dangers of hypoxia due to sustained uterine contractions.

4. It is questionable if the lower uterine segment cesarean section should be performed when this syndrome may be encountered, and if this type of cesarean section is done, the incision should not be a transverse one.

5. Multiple uterine incisions cause marked postoperative pain.

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Comments by Percy Malpas, M.D., of Liverpool, England

Over and above its theoretical implications, this presentation does set out clearly the practical problem of delivering a shoulder presentation through a transverse lower segment incision when the uterus is contracting strongly. A similar difficulty can of course arise with any form of anesthesia in which the reactivity of the myometrium is unimpaired, local for instance, or a Pentothal Sodium, curare, and light ether anesthesia. In a personal and quite comparable case performed under the latter, a median upward incision had hurriedly to be made to extract the baby. I know of another case in which a difficult extraction was persevered with through a transverse incision, and which resulted in a fatal hemorrhage from torn uterine vessels.

The uterine response is the same whether a spinal anesthetic or a light general or local anesthetic is employed, the difference being that with spinal anesthesia the onset of the strong contractions is spontaneous; with local or the light general anesthesia which is possible when curare is used the contraction which causes the difficulty is secondary to the handling of the uterus.

Most obstetricians would agree with the contention that the choice lies between a primary median incision and a general anesthetic of such depth that the myometrium is rendered inert. Most would choose the former course.

The problem of the mechanism of the release of uterine contractions at term is obscure. The myometrial reactivity increases as term approaches, and reaches a maximum at the expected date of delivery, thereafter tending to abate. Whether this increased reactivity is a specific pregnancy phenomenon, or whether it is the result merely of increasing uterine tension, is still unsettled. In some ways it may be unsound to regard the uterus as obeying other laws than those that regulate the other hollow autonomic excretory viscera. If this is so the onset of labor is to be regarded as due to the liberation of contractions when the inhibiting factors which allow pregnancy to continue are lifted.

The authors' findings seem to support the view that the inhibition is nervous and not humoral or hormonal. Such a view also conforms better with the rapidity with which labor starts once a critical point is reached, and is also supported by the relative failure of all attempts to inhibit uterine contractions in vivo by the exhibition of the supposedly inhibitory hormones. As knowledge increases there may be developed an acceptable synthesis of both theories.

REPAIR OF ENTEROCELE WITH PRESERVATION OF THE VAGINA

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ENTEROCELE is ordinarily produced by injury during childbirth. The injury differs from that which is responsible for rectocele in that it is located higher in the posterior vaginal wall. Enterocele is a definite hernia with a sac lined by peritoneum and containing abdominal contents. Careful dissection during the repair of enterocele or during the performance of abdominoperineal resections of the rectum in women will disclose that the space through which the hernia occurs in enterocele is bounded superiorly by the posterior rim of the cervix, laterally by the uterosacral ligaments, and inferiorly by the levator ani muscles. A rupture of the endopelvic fascia has permitted an elongation of the cul-de-sac of Douglas to form the hernial sac. The intestines gravitate into the sac and, as the intra-abdominal pressure continues to exert an effect upon this sac, it becomes larger and larger. Usually, the uterus descends somewhat during the development of the enterocele, probably because there is a general weakening of elastic tissue supports as age progresses, with a relaxation and elongation of all the ligaments attached to the uterus. These findings refute to a great extent, the theory of Moschowitz[1] that a deepening of the cul-de-sac was responsible for procidentia of the rectum. Procidentia requires incompetence of the anal sphincter. In order to cure enterocele properly, one must obliterate the weakened space through which the peritoneal contents herniate. This space can best be obliterated when the uterus has been removed vaginally. Then the cardinal ligaments, uterosacral ligaments, and the levator ani muscles can be united. The vagina becomes shortened to a certain extent as a result of the repair, and it is wise to inform the patient of this possibility.

Technique

A vaginal hysterectomy is performed in the usual manner, but the ligatures on the uterosacral ligaments and the cardinal ligaments are separately marked and left long. The cystocele and the urethrocele, which usually accompany the prolapse and enterocele, are properly repaired by wide dissection of the bladder and plication of the bladder and urethra by the Kennedy[2] technique. The broad and round ligaments are united in the midline and stitched to the periosteum of the pubis. The peritoneum is closed very high posteriorly by putting marked traction on the uterosacral ligaments. The redundant mucosa is then excised and the anterior vaginal wall is sutured in the midline with either interrupted chromic catgut sutures or a continuous locked chromic catgut stitch. The cardinal ligaments are then brought together in the midline and then, with traction on the uterosacral ligaments, they are sutured to these ligaments in such a manner as to bring the uterosacral ligaments together where

this union is made. The posterior vaginal repair is then begun. The mucosa is dissected to a point within one inch of the original opening through which the uterus was removed. The mucosa is freed of underlying fascia and the levator ani muscles are exposed. These muscles are united in the midline as high as possible. The bridge of vaginal mucosa remaining is then undermined and the sutures attached to the uterosacral ligaments are brought out beneath the bridge of mucosa and united to the levator ani muscles. This latter procedure completely obliterates the hernial opening. The levator ani muscles are further united. The redundant mucosa of the posterior vaginal wall is excised and the cut edges, perineal muscles, and skin are sutured in the usual manner of repair of the posterior vaginal wall for rectocele.

A small enterocele may be repaired with preservation of the uterus but the uterosacral ligaments and cardinal ligaments cannot be utilized to close the hernial defect. In such instances, the dissection of the mucosa of the posterior vaginal wall is carried as high as possible, and the remaining bridge between the posterior rim of the cervix and apex of the triangular defect produced by excision of mucosa is undermined. When the levator ani muscles are united as high as possible both ends of the stitch are left long. The ends of the stitch are then separately threaded on needles and each end is carried beneath the bridge of mucosa to penetrate it as near to the cervix as possible. When the two ends are tied, a mattress stitch is formed which transplants the united levator ani muscles up under the bridge of mucosa. The remainder of the repair is completed as for rectocele. Anatomically and clinically, the results are inferior to those obtained by the method utilized when the uterus is removed. When large enterocele is present, the uterus must be removed and the defect properly closed as described above to accomplish a cure.

Case Reports

CASE 1.—F. K., a white woman, aged 59 years, was admitted to the hospital Nov. 26, 1951, and discharged Dec. 12, 1951. The chief complaints were burning in midepigastrium, abdominal distention, and protrusion from the vagina. The onset of her menstrual periods was at age 17, and menopause was at 47. She was a para iii, gravida vi.

Physical examination: Pulse 88, blood pressure 160/100, a systolic murmur at the mitral valve area of the heart. The rate and rhythm were normal, and there was no enlargement. There was marked diastasis of the rectus muscles of the upper abdomen. She had a reducible umbilical hernia, marked herniation through the vagina on straining.

Laboratory findings: Hemoglobin 14 Gm. white blood count 8,350. Urinalysis: color amber, specific gravity 1.202, reaction acid, albumin two plus, sugar negative, and microscopically a few epithelial cells and bacteria. Nonprotein nitrogen was 36.8, blood chlorides 462, blood carbon dioxide combining power 65.1 c.c.

X-ray reports: Normally functioning gall bladder, marked rotatory lateral scoliosis of dorsolumbar spine, no evidence of organic disease of the esophagus, stomach, or duodenum.

Surgery: Nov. 10, 1951. Repair of marked diastasis of the rectus muscles of the upper abdomen, repair of umbilical hernia, vaginal hysterectomy with repair of cystocele and large enterocele as described above. Spinal and intravenous Pentothal Sodium anesthesia used.

Pathological report: Retrogressed hyperplasia of endometrium with superficial hemorrhages, adenomyosis of the uterus, subinvolution of the uterus, glandular hyperplastic endocervicitis with erosion, multiple Nabothian cysts, and vaginal flaps.

Postoperative course: Temperature 102° F. on the seventh day. Penicillin was given, but it produced a skin rash, some urinary symptoms developed, which disappeared, and the patient left the hospital in good condition on the twelfth day. The anatomical and clinical results to date have been excellent.

CASE 2.—F. H., a white woman, aged 62 years, was admitted to the hospital, Jan. 15, 1952.

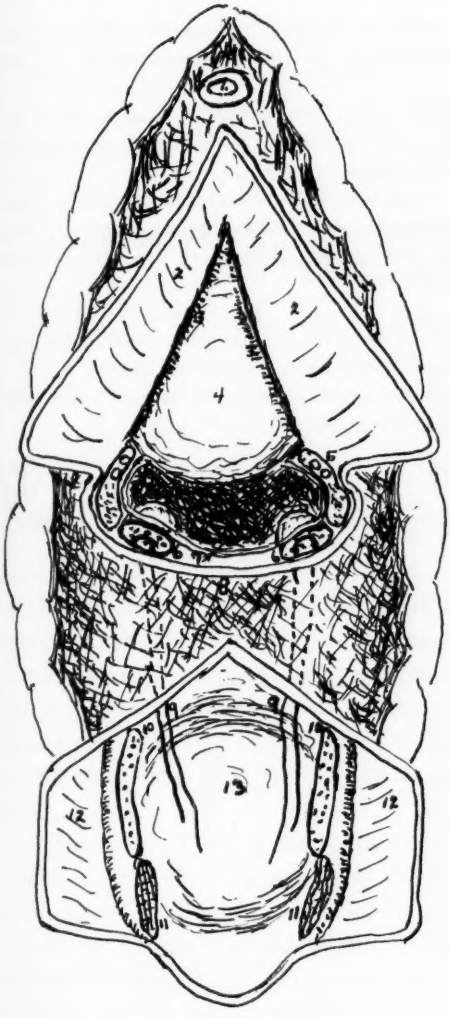

Fig. 1.

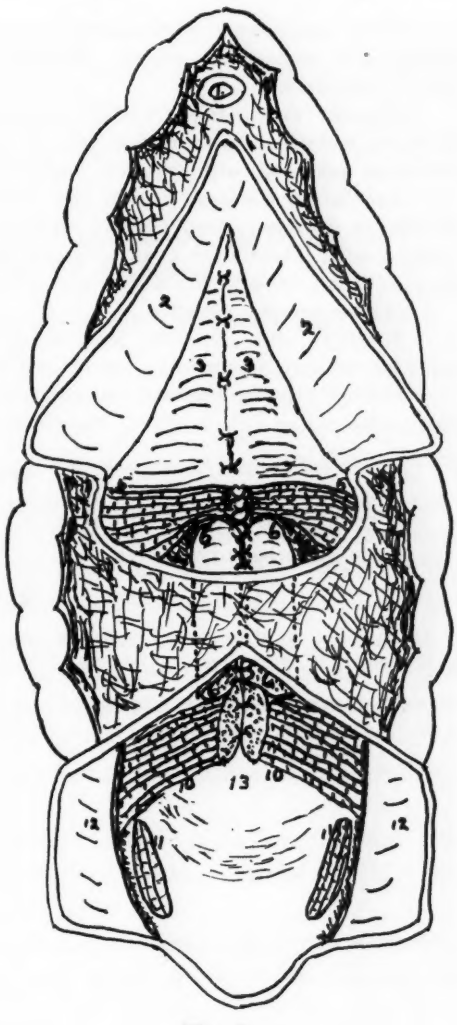

Fig. 2.

Fig. 1.*—Shows the uterus removed; the uterosacral ligaments secured *separately* from the cardinal ligaments; the bladder dissected free in the region of the cystocele; and the dissection of the posterior vaginal wall with the ligatures attached to the uterosacral ligaments brought out beneath the bridge of mucosa preserved between the posterior wall of the vagina and the orifice formerly occupied by the uterus. All other ligatures, retractors, and clamps are omitted to avoid confusion. During the actual operation, the posterior vaginal wall dissection is not begun until the peritoneum has been closed, while an assistant makes strong traction on the uterosacral ligatures; the cardinal ligaments have been united and sutured high on the united uterosacral ligaments; the cystocele and urethrocele, if present, have been repaired; the excess mucous membrane of the anterior vaginal wall has been excised; and the edges of the mucous membrane united down to the orifice formerly occupied by the uterus.

Fig. 2.*—Shows the disposition of the cardinal and uterosacral ligaments and the levator ani muscles. By this time the cystocele repair is usually completed. Actual union of the uterosacral ligaments and levator ani muscles is usually accomplished beneath the bridge of mucosa left high on the posterior vaginal wall. If mucosa is redundant in this area, a part of the bridge may be excised.

*Key:

1. Urethra
2. Flaps of mucous membrane of anterior vaginal wall
3. Fascia
4. Bladder
5. Cardinal ligaments
6. Uterosacral ligaments
7. Peritoneum
8. Space where enterocele emerges
9. Suture ligatures through uterosacral ligaments brought out beneath bridge of vaginal mucous membrane on posterior wall
10. Levator ani muscles
11. Perineal muscles
12. Flaps of mucous membrane of posterior vaginal wall
13. Area of rectocele

Chief complaints: "Womb comes out for past 3 or 4 years," frequency of urination, constipation, some ankle edema. History: Appendectomy in 1920, menopause at age 49, para i, gravida i.

Physical examination: Blood pressure 160/98, pulse 80, positive findings consisted of an appendectomy scar, variocosities of both legs, mild edema of both ankles, and marked enterocele associated with cystocele, urethrocele, and prolapse of uterus.

Laboratory findings: Kahn and Klein tests negative, white blood count 12,250, hemoglobin—16 Gm., red blood count 4,730,000. Urinalysis: color yellow, specific gravity 1.025, reaction acid, albumin trace, sugar negative, and microscopically there were two plus bacteria present. Nonprotein nitrogen 39.5 and blood sugar 112.

Chest x-ray was negative.

Surgery: Jan. 17, 1952, under nitrous oxide, ether, and cyclopropane anesthesia, vaginal hysterectomy, repair of cystocele, urethrocele, and enterocele as described above.

Postoperative course was marred only by pleurisy on the tenth postoperative day. She was discharged on Feb. 2, 1952. The result to date has been excellent.

Summary

A technique for the repair of a very large enterocele is presented. Illustrative cases are also presented.

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A PROPOSED CLASSIFICATION FOR CASES OF CANCER OF THE CERVIX TREATED BY SURGERY

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WITH the renewed interest in the surgical treatment of cancer of the cervix and the recognition of the principle that such treatment in the modern sense includes a systematic pelvic node and areolar tissue excision, and the fact that there is thus obtained a complex surgical specimen for pathologic study, it becomes apparent that a classification based upon surgical pathologic findings becomes necessary. In developing such a classification it is not implied that it should replace, compete with, or confuse the present International Classification which is based purely upon clinical findings and employable for comparison of results obtained by irradiation therapy. The International Classification serves its purpose well, but has the limitations of not being substantiated by histologic study.

It is obvious that the present International Classification is inadequate for cataloguing and comparison of surgical results because the clinical findings are so often not confirmed by histopathologic findings.

In an attempt to establish a common basis for discussion of surgical results, the pathologic classification described below and based upon actual study of the surgical specimens is suggested.

The shortcomings are obvious in that it is impractical to secure complete serial sections of all tissue removed and thus some margin of error is inevitable, but this deficiency is inherent in any system of pathologic classification devised as a practical method of study.

The classification was set up and a number of interested and prominent workers in the field were consulted. Suggestions received were carefully reviewed and incorporated where feasible.

Inasmuch as this classification is for evaluation of surgical results, the situation obtaining at the time of operation is the prime concern. Where, for example, a patient has received irradiation therapy after positive biopsy, and then been operated upon, and the surgical specimen fails upon reasonably thorough study to show the presence of carcinoma, that patient is classifiable in this system because of the positive biopsy also, if such a patient should die after operation, her death certainly would be classified as a surgical death. Survival cannot, with assurance, be attributed to surgical effort and thus should be placed in a special surgical category.

Another category of patients not as yet and here classified are those who prove to have lymph node metastases outside the pelvis.

In the classification of surgical specimens it is obviously necessary that the surgeon cooperate with the pathologist to the extent of accurately describing the sites of the nodes and areolar tissues removed.

In order to avoid confusion with the International Clinical Classification, classes, not stages, are used, and letters of the alphabet instead of numerals to designate various stages are employed.

Surgical and Pathologic Classification of Carcinoma of the Uterine Cervix

Class O.—Carcinoma in situ, also known as preinvasive carcinoma, intraepithelial carcinoma, microcarcinoma.

Class A.—The carcinoma is strictly confined to the cervix.

Class Ao.—After a positive biopsy of infiltrating carcinoma, no tumor is found in the cervix in the surgical specimen.

Class B.—The carcinoma extends from the cervix to involve the vagina, except lower third. The carcinoma extends into the corpus. The carcinoma may involve the upper vagina and corpus. Vaginal and/or uterine extension may be by direct spread or be metastatic.

Class C.—The carcinoma has involved paracervical and/or paravaginal tissue by direct extension or by lymphatic vessels, or in nodes within such tissues. Vaginal metastases and/or direct extension into the lower third of the vagina.

Class D.—Lymph vessel and node involvement beyond paracervical and paravaginal regions. This includes all lymphatic vessels and/or nodes in the true pelvis, except as described in *Class C.* Metastasis to the ovary or tube.

Class E.—The carcinoma has penetrated to the serosa, musculature, or mucosa of the bladder and/or of the colon or rectum.

Class F.—The carcinoma involves the pelvic wall (fascia, muscle, bone, and/or sacral plexus).

Adenocarcinomas of the cervix are classified as above; no differentiation is made from epidermoid carcinoma. At present carcinoma of the stump is considered in the same manner as cancer of the cervix with the uterus intact.

In the event of preoperative irradiation, if the neoplasm has disappeared from the cervix but is still present in extracervical pelvic structures, the situation is classified according to the limits of the extent of the extracervical spread.

Since, in the opinion of some workers, planned preoperative irradiation is given and at a stated period after this treatment operation is performed, a special category for these patients is necessary, therefore, it is suggested that the prefix PR (preoperative irradiation) be placed before the above classifications. On the other hand, operation may be performed after failure of irradiation administered as a curative treatment. This would constitute another category and it is suggested that the prefix R (irradiation) be placed before the designated class found at surgical operation.

A third category of patients are those who present recurrence after previous surgical attempt to eradicate the disease and it is suggested that the prefix S (surgical) be employed. Still a fourth category of patients are those who have had both irradiation and surgery employed, each of which attempts were made envisaging cure but who finally present themselves for further surgery. It is suggested that the prefix RS (irradiation and surgery) be employed.

This classification may appear at first glance to be quite complex, especially when compared with the rather simple and forthright International Classification in which five groups only are proposed. However, in the above suggested classification, all situations that the surgeon is confronted with are covered. This would seem necessary since the surgical treatment may be attempted under a variety of situations, viz., as primary treatment, as treatment following preoperative irradiation, and as an attempt to control the disease after previous failures by irradiation and/or surgery. Obviously, where surgery is the primary method of treatment, classification of the patients would be relatively simple.

As examples, hypothetical situations are described below and their classification determined:

A. A patient with carcinoma apparently limited to the cervix, International Classification Stage I. After radical hysterectomy and pelvic node excision the pathological report states: Epidermoid carcinoma of cervix with cervical lymph vessel permeation, pelvic nodes negative.

Surgical and pathological classification: Class A.—

B. A patient received preoperative irradiation and hysterectomy with pelvic lymph node excision six weeks after last irradiation treatment. The pathologic report stated that there was no evidence of carcinoma in the cervix but there was metastatic epidermoid carcinoma in right obturator node.

Surgical and pathological classification: Class PRD.—

C. A patient received 6,000 mg. hr. of radium to the cervix and 12,000 r total dose of x-ray therapy to six pelvic ports three years previously. One year later recurrence developed for which a so-called Wertheim hysterectomy was performed. Two years later fungating epidermoid carcinoma was found in the upper third of the vagina. For this total vaginectomy and pelvic lymph node excision was carried out. Pathologic report: epidermoid carcinoma in upper third of vagina and metastases to both groups of obturator nodes and hypogastric nodes.

Surgical and pathological classification: Class RSD.—

D. The patient had no previous treatment and was found to have a large, ulcerating lesion replacing the cervix with so-called "frozen pelvis." Pelvic exenteration was carried out during which frozen section biopsy of thickened fascia over right levator ani muscle was reported as showing epidermoid carcinoma.

Surgical and pathological classification: Class F.—

To repeat, the suggested classification might appear unduly complex and yet some basis for common discussion of these patients is necessary. It is obvious that patients who receive operation having their carcinoma confined to the cervix are in a separate category from those who receive operation after planned preoperative irradiation therapy, and each of these groups is different from those who received operation after irradiation was administered in attempt to eradicate the disease but failed to do so, and still in a different category are those who receive operation after preoperative irradiation and multiple sections reveal no residual carcinoma.

Summary

A classification is presented to catalogue patients with carcinoma of the cervix who receive radical hysterectomy and pelvic lymph node excision or some type of pelvic exenteration operation. The need for such a classification is presented.

THE USE OF MENADIONE BISULFITE AND ASCORBIC ACID IN THE TREATMENT OF NAUSEA AND VOMITING OF PREGNANCY

A Preliminary Report

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THE object of this study was to find an effective, simple, and inexpensive treatment for the nausea and vomiting of pregnancy.

The causes of nausea and vomiting of early pregnancy are unknown. Hypotheses which stressed such mechanisms as emotion and physical shocks, excessive protein in the maternal diet, and fanciful exogenous factors are rapidly receding into the folklore of medicine. Current theories include the possible presence of a fetal or placental toxin, or some disturbance of hormonal equilibrium.[1] Bertling[2] attributed nausea and vomiting of pregnancy to inadequate utilization of chorionic gonadotropin. According to Vanden Bosch[3] it may be caused by a temporary depression of adrenal function.

These postulates are merely suggestive. The only observation with which all physicians will agree is that the disorder is more common in high-strung women with neurotic backgrounds than in those women who are reserved and less sensitive.

While physical factors are undoubtedly concerned, this observation suggests that there is also a large psychogenic component in the vomiting of pregnancy. There are many women who do not want to become pregnant. However, it is impossible to say to what extent the vomiting of pregnancy is due to a physical factor or to what extent it is due to a psychological cause. As in so many other psychosomatic problems, both factors probably operate in most cases, their relative proportion depending upon the psychosomatic characteristics of the individual.

The author postulates that the occurrence of nausea and/or vomiting of pregnancy depends upon the transfer of a vomiting factor from the placenta or fetal circulation to the expectant mother, and that the cause of this transfer in many women is some abnormality, functional or organic, in the placenta or its uterine base. It is further reasoned that a most important cause of "vomiting factor" transfer is due to an increased capillary permeability in the placental base.

In the treatment of nausea and vomiting of pregnancy, the importance of hydration and dehydration is well established. Bertling[2] used diethylstilbestrol, since, by causing an increase of progesterone secretion, the utilization of chorionic gonadotropin is facilitated. Titus[4] recommended mental rest, sedation, and a high carbohydrate-high vitamin B and C diet. Kroger and

DeLee[5] used hypnosis successfully in seventeen of nineteen cases. Antihistaminics were suggested by Dougray.[6]

Material

In the investigation herewith reported, ascorbic acid, U.S.P.,* and menadione bisulfite (synthetic vitamin K), U.S.P.,* were used to decrease placental capillary permeability, thereby preventing transfer of the "vomiting factor" to the expectant mother. This treatment was used in a series of seventy consecutive cases of nausea and/or vomiting of pregnancy, varying from mild to severe. Thirty-three of the women were primigravidas and thirty-seven multigravidas. Seven were Rh negative, and sixty-three Rh positive. All were given orally each day 25 mg. of ascorbic acid and 5 mg. of menadione bisulfite without any attempt at psychotherapy or other supportive measures. The prothrombin levels in the blood and the bleeding time of each patient were determined both prior to medication and afterward.†

Therapy, averaging thirty days, was continued until the withdrawal of medication produced no recurrence of symptoms.

Results

Sixty-four patients reported complete remission of symptoms within seventy-two hours. Three were relieved of their vomiting, but continued to have nausea after prolonged and increased amounts of medication. Three received no apparent relief of their nausea and/or vomiting. In an advanced case of hyperemesis gravidarum in the second trimester, and a case of pseudocyesis, this medication appeared to be dramatically beneficial when other means of treatment had failed. Three patients required continual medication until delivery.

Preliminary studies with ascorbic acid alone revealed little improvement in nausea and/or vomiting, while studies with menadione bisulfite alone showed improvement in about 50 per cent of the cases. During this study it became apparent that oral iron therapy used in the treatment of anemia of pregnancy caused little or no gastrointestinal disturbance, and iron absorption was enhanced by the vitamin C and K therapy.[7]

Comment

The treatment of nausea and vomiting of pregnancy still constitutes a major problem in antenatal care. It is well recognized that spontaneous relief of symptoms may be expected by the end of the first trimester of pregnancy. Accordingly, great care must be exercised in evaluating the results of any treatment at or after this period.

Allowing for the fact that some of these patients could have expected eventual relief without treatment, it is difficult not to be impressed with the results obtained. At any rate, the success of this method has made it desirable to carry the investigation further. This addition to the already voluminous writing on the subject seems justified on the ground that the suggested method of treatment combines greater effectiveness and simplicity than do other methods now in vogue.

Pharmacologic studies‡ on menadione bisulfite carried out in the Abbott Laboratories indicate that its toxicity is relatively low. In man, doses approximately ten times as great as those generally recommended for therapeutic use, given daily for a period of one week, induced no significant changes in

*Supplied by the Abbott Laboratories, North Chicago, Ill.
†All tests were carried out in the Lattimore-Fink Laboratory, Topeka, Kan.
‡These pharmacologic data were supplied by the manufacturer.

the blood. The prothrombin levels and bleeding time of each patient determined both prior to medication and after were normal.

Summary

1. A new, effective, simple, and inexpensive treatment for nausea and/or vomiting of pregnancy is described.

2. A study of seventy consecutive cases of nausea and vomiting in early pregnancy treated with menadione bisulfite and ascorbic acid is presented.

3. In all cases the prothrombin levels and bleeding time were normal both before and after medication.

4. It is suggested that this therapy may be of value in the reduction of gastrointestinal symptoms following the ingestion of iron salts used in the treatment of anemia of pregnancy.

5. Menadione bisulfite or ascorbic acid alone failed to give satisfactory relief from nausea and/or vomiting of pregnancy.

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THE MANAGEMENT OF THE THIRD STAGE OF LABOR EMPLOYING A COMBINATION OF PITOCIN AND METHYLERGONOVINE (METHERGINE)

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IN THE last few years two main oxytocics have been available for use in the third stage of labor; pituitary extracts and ergot preparations. Articles showing the main advantages of each are abundant in the literature. However, I have found that the third stage of labor can be simplified and blood loss kept at a minimum by combining two types of oxytocics.

DeLee[1] pointed out the advantages as well as the harmful effects of posterior pituitary extract. He began using, in 1940, "ergonovine to back up the action of solution of posterior pituitary." Greenhill[2] also discussed the benefits observed following the routine use of pituitary extract and ergot or ergonovine after the placenta has been expelled. Leff[3] describes his method for the management of the third stage of labor. He first injects 1 ampul of Pitocin (10 units) and after 20 minutes gives 1 ampul (0.2 mg.) of Ergotrate intramuscularly. In this way, he obtains contraction of the uterus with retraction of the cervix and a firm tonic uterus. However, we did not find a large number of articles on the use of the combination in the literature.

As far as we know this is the first detailed description of the use of Pitocin in combination with Methergine. Methergine is a recently developed semisynthetic ergot alkaloid. Chemically, it is methylergonovine tartrate obtained by synthesis of lysergic acid and 2-aminobutanol.[4] It possesses the same properties as ergonovine. Quantitatively, it is long acting and prompt in onset.[5, 6, 7, 8] In addition, it is known not to have any demonstrable side effects nor does it show any systemic action on blood pressure or pulse rate.[9] It is equally as effective as ergonovine in maintaining blood loss at a minimum.[10] In one instance, particularly, it was most effective in contracting the uterus promptly in a case of severe hemorrhage.

Method

Shortly before delivery, if time permits, atropine sulfate $\frac{1}{150}$ grain (0.4 mg.) is given by hypodermic routinely. After the baby is born, 1 c.c. (10 units) of Pitocin intramuscularly, never intravenously in this concentrated form, is administered. Within 3 to 5 minutes the placenta is delivered. We do not employ a manual removal of the placenta but have adopted a modification of Credé's delivery. Once the placenta has been delivered Methergine 1 c.c. (0.2 mg.) intravenously or intramuscularly is administered. The uterus stays contracted and there is usually very little bleeding. If excessive bleeding does occur, it usually happens in those cases where the episiotomy is rather extensive.

In cesarean sections Pitocin intramuscularly is administered after the peritoneum is opened and we are about ready to start the low bladder flap. One c.c. of Methergine (0.2 mg.) intravenously is administered as soon as the

baby is taken from the uterus. We never use morphine preoperatively, but use it following cesarean after the patient has returned to her room.

In breech and forceps delivery, as well as when twins are delivered, the same amount of both Pitocin and Methergine as designated in the standard procedure is employed. With twins however, Pitocin is injected intramuscularly as soon as the second twin is delivered. Occasionally, however, if the uterus shows no activity and is atonic, ½ minim to 1 minim of Pitocin is administered intramuscularly before the birth of the second twin.

In cases of eclampsia or pre-eclampsia Pitocin is employed because it has little or no effect on the blood pressure. It is administered as soon as the baby is delivered and is followed by 1 c.c. of Methergine after placental delivery. In vaginal delivery in cases of placenta previa the method is as usual.

In all instances oral tablets of Methergine are started on the day of delivery, after the nausea is over, and are given three times a day until 6 tablets have been taken. If the fundus is not firm and the lochia is excessive and foul, an additional 6 doses are prescribed. However, it has been our experience that in most cases only the first 6 doses are necessary. In most of our cases, drop ether is employed at the time of episiotomy or started just before the child is delivered. This does not appear to affect, in any way, the effectiveness of Methergine. In many instances we have also found it very useful to administer Seconal (1½ to 3 grains) or Demerol (100 mg. or 2 c.c.) or both in order to quiet and relax the patient during labor; occasionally, both are repeated. We have found that scopolamine tends to make the patient more difficult to restrain and it is not used routinely in our deliveries.

The patients are treated as above and usually remain in the hospital 5 to 7 days. They are allowed to sit up on the first postpartum day if there are no complaints or complications, and to get out of bed on the second postpartum day.

Results

This report includes 135 cases treated in the above manner. Our study is summarized in Table I.

TABLE I

1. Parity.—	
Para i	59
Para ii	50
Para iii	15
Para iv	9
Para v	2
2. Age Group.—	
18-24	48
25-30	52
31-35	26
36-40	9
3. Method of Delivery.—	
Spontaneous	99
Cesarean	9
Breech	6
Midforceps	1
Low forceps	20
4. Blood Loss.—	
Normal loss of blood	108
Slight loss in excess of normal	10
Moderate bleeding	15
Severe bleeding because of friable tissues	1
Severe bleeding associated with first degree laceration	1
5. Injections.—	
Two injections of Pitocin required	1
Two injections of Methergine required	4

The number of cesareans listed above includes those cases from my personal practice combined with those of other doctors on which I acted as an assistant. The incidence of cesarean at our hospital for the year 1950 was 2.7 per cent from a total of over 900 deliveries.

We have used Methergine because, in our experience, the fundus became firm, there were no retained placentas, there was no excessive bleeding, there were no blood pressure changes, and oral tablets were effective in increasing the rate of involution post partum. Methergine is not toxic; there is no danger of sloughing with an overdose so that oral tablets can be continued until bleeding is stopped and involution is completed. The uterus stays firm. There is little complaint of afterpains with Methergine.

This method of employing Pitocin and Methergine is helpful in a smaller hospital where there is only one physician and one nurse to deliver the baby. With conditions as they are, and the lack of help so marked in many hospitals throughout the country, it was felt that a method, such as this, is desirable which facilitates delivery with as few physicians and nurses as possible. When Pitocin is given following the birth of the child the uterus contracts. Within 3 to 5 minutes the placenta is delivered and the uterus begins to relax as the effect of Pitocin wears off. When Methergine is given following the delivery of the placenta a second contraction of the uterus occurs, thus causing it to become small, hard, and involuted. Within 3 to 5 minutes following an injection of 1 c.c. Pitocin in most instances, and never any longer than 15 minutes, the placenta is delivered. In that time the physician is free to clean the mucus from the baby's throat and nose, tie the cord, wipe the baby off, warm him, and get him started in life. A nurse watches the descent of the uterus by keeping her hands on the uterus, through the abdomen one below and one on the fundus, so that the physician is free to devote his time to the care of the baby. As soon as he has finished this he can deliver the placenta, repair the episiotomy, and see that the patient is in good condition. With this method the uterus involutes rapidly. Bleeding has been kept to a minimum, and in general the delivery is handled easily.

Conclusions

1. We have described a method of delivery in which 1 c.c. of Pitocin is given following the delivery of the child.

2. One c.c. of Methergine is administered either intravenously or intramuscularly following the delivery of the placenta.

3. In this way, the physician with one nurse can completely manage delivery and adequately take care of both the mother and the child.

4. Methergine is an effective, long-lasting, dependable oxytocic which makes the uterus firm and keeps it firm. In addition, oral Methergine tablets can be used post partum without any danger of side effects or toxicity.

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OSTEOGENIC SARCOMA OF THE OVARY

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THERE are numerous reports of extraskeletal osteogenic sarcoma in the literature and some organs (e.g., the thyroid) seem to be the sites of a disproportionate number of the tumors described. The ovary, while it is notorious as an organ in which tumors are seen which bear little or no relationship to its normal features, has figured in only one previous instance of osteogenic sarcoma,[1, 2] although ossification of various ovarian tumors is far from unknown, and the development of bone structure is seen not infrequently in teratomas. Selye[3] suggests that it is questionable whether true primary osteogenic sarcoma can originate in the ovary, feeling that some other origin, such as that from teratoma, is likely. The case to be reported has certain features which tend to confirm this view.

Donati's case, reported in 1904, was that of a 36-year-old woman whose complaint was of pain, located in the right inguinal region and in the right lower quadrant. She had also noted abdominal enlargement; menses were regular. At operation a right-sided ovarian tumor was found; this filled the entire abdomen. Microscopically the tumor had the features of osteosarcoma. There is no description of features which might point to a teratomatous origin.

Case Report.—Mrs. S. C., S.U.H. No. 294922, aged 67 years, was well until 1945 when she first noted a mass in the right inguinal region. This did not change and she did nothing about it until 1947 when she consulted a physician who told her she had a hernia and advised the wearing of a truss. This she did not do until about four months before admission, 1951, when she went to a truss maker. The latter told her that she did not have a hernia but rather some sort of tumor mass, and advised her to see a physician. After a delay of two months she did this; the impression was confirmed and the patient was referred to this hospital, where she was first seen some two months later. She was not conscious of material change in the mass during the time after it had first appeared, and had been well except for rather minor weight loss, and occasional mild lower abdominal cramps which had been noted intermittently for the month preceding admission.

On admission to the hospital the patient appeared chronically ill. The blood pressure was 154/106; temperature, pulse, and respirations were normal. The head, neck, chest, and extremities showed no unusual findings. In the abdomen could be felt very firm, nodular masses rising in both lower quadrants to the level of the umbilicus. These were fixed, and were not tender. In the right inguinal area there was a similar very hard, nodular mass measuring 5 cm. in greatest diameter which was freely movable. Pelvic examination showed a well-supported parous outlet. The vagina and cervix were not remarkable. The uterus and adnexa could not be made out as structures separate from an irregular, nodular, hard mass which filled

the cul-de-sac and extended to the lateral pelvic wall on each side and which rose superiorly to blend with the masses noted in the abdomen. A diagnosis of ovarian carcinoma with abdominal extension was made, and laparotomy was advised.

At operation the inguinal area was explored and a right indirect inguinal hernia was found. In the sac was an obvious tumor mass 2 to 3 cm. in diameter. When the abdomen was opened a very large tumor mass was found arising from the right adnexa. The entire lower abdomen was filled with the mass, and a large cystic portion extended into the upper abdomen almost to the level of the diaphragm. The mass was removed together with the uterus and adnexa. Many metastatic nodules were found in the omentum, the parietal peritoneum, the mesentery of the bowel, and over the surfaces of both large and small intestines. Some of these nodules were also removed. The liver was free of involvement.

The patient had an uneventful postoperative course and was discharged on the tenth postoperative day. Because of the pathologic diagnosis of osteogenic sarcoma of the ovary (see below) studies of calcium and phosphorus were made; these values fell within the normal range. X-rays of the abdomen showed calcification to be scattered throughout many parts of the lower abdomen; this was interpreted as visualization of the many nodules which had to be left in situ.

The patient was seen about six weeks after operation at which time she felt well. However, there was a marked progression of the tumor in the abdomen; a number of large, stony-hard nodules could be felt with ease. Shortly thereafter she passed into the hands of a private physician, and was admitted to another hospital about five months after operation for terminal care. She is reported to have been markedly cachectic and to have had ascites and a very large, hard liver. Since there were some elements of cardiac failure at the end, it is not clear whether these abdominal findings were due to the tumor alone. No postmortem examination was made.

Pathologic examination of the material removed at operation showed a large, very irregular tumor mass, together with the uterus, the left adnexa, and a number of metastatic nodules. Neither grossly nor microscopically were there unusual findings in the uterus and left adnexa. The large mass measured approximately 15 cm. in diameter. It was partly cystic and partly solid. The solid component made up about two-fifths of the total mass, and was stony hard. It was irregularly nodular but the surface was smooth and rather creamy white in color. Several areas showed hemorrhagic mottling. Attached to the solid portion of the tumor by broad bases were two quite large, and several smaller, cystic structures. These had smooth, translucent walls through which a deep blue-black color could be seen. One of the large cysts had ruptured. On section most of the solid portions of the tumor were found to be well calcified, and suggested soft bone. Minute sharp, hard spicules could be felt on the cut surface. Parts of the solid tumor were firm and rubbery in consistency, and had some irregular yellow mottling, as well as a number of small cysts with smooth gray linings. The cystic portions of the tumor were found to be loculated, and to contain clear, almost black, thin fluid. The cyst linings were smooth. The metastatic masses taken from the omentum, the peritoneum, and the hernial sac were similar in appearance to the solid portion of the main tumor.

Microscopically the solid portions of the tumor show two separate pictures. The sections taken from the calcified areas of the solid portions of the tumor show the characteristic features of osteogenic sarcoma. In most areas the process is proceeding in an orderly fashion as seen in Fig. 1. In the greater part of the tumor the bony trabeculae are forming in a poorly defined osteoid matrix, while in some areas there are cartilaginous islands as well as osteoid tissue. In such instances there is little evidence of bone formation in the cartilaginous portions.

Fig. 2 shows details of the bone formation about one of the bony trabeculae. Osteoblasts are grouped about the bone in a normal fashion, but the surrounding osteoid tissue shows little in the way of matrix, and is poorly organized.

In Figs. 3 and 4 other parts of the bony portion of the tumor are seen. The organization is extremely poor, and osteoclastic giant-cell activity seems evident near the poorly-formed trabeculae. Nevertheless, osteoblasts are also in evidence. The degree of calcification

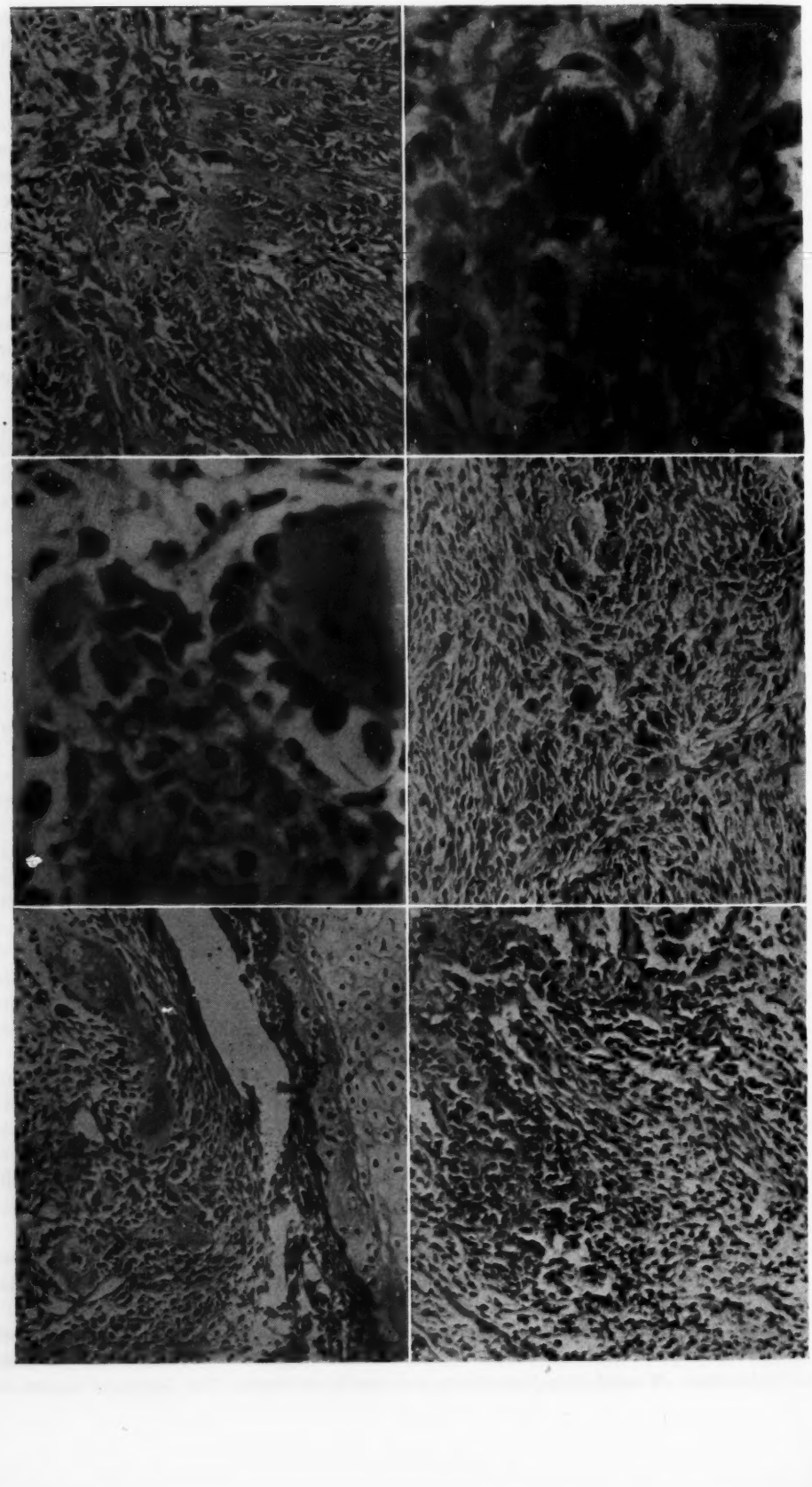

Fig. 1.

Fig. 2.

Fig. 3.

Fig. 4.

Fig. 5.

Fig. 6.

of the trabeculae is limited, and the calcification shades off into the fibrous portion of the tumor without a distinct line of demarcation. Figs. 5 and 6 show some of the many giant cells which were scattered throughout the solid portions of the tumor. They were more prominent in the less well-calcified areas. Such cells are frequently seen in the osteogenic sarcomas of bone, and were noted by Donati in the ovarian tumor described by him.[1, 2]

Fig. 7.

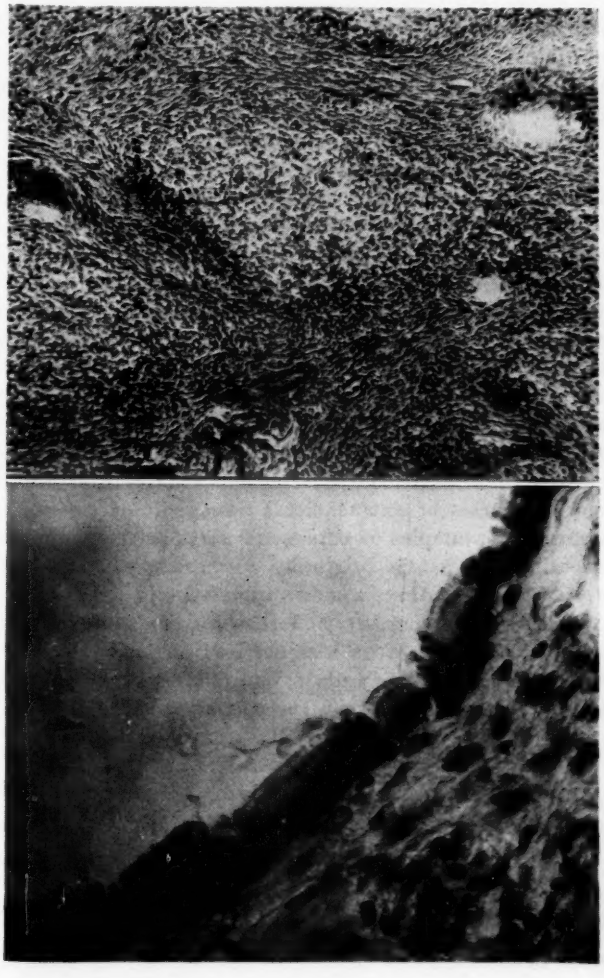

Fig. 8.

The solid elastic parts of the tumor consist of a fairly dense fibrous structure in which the individual cells have little evidence of malignancy. Occasional bizarre forms are noted, but, with the exception of a feature to be commented upon, the tissue, while neoplastic, has an appearance quite similar to that of a fibroma of the ovary; its features can be seen in the nonepithelial portions of Fig. 8. The single remarkable feature is the presence of irregular islands of spindle cells having little cytoplasm and associated with almost no fibrils or collagen. The nuclei of these cells appear wrinkled and folded, in contrast to the smooth outline of the nuclei of the surrounding cells. Each of the islands seems to be based on a small vessel, but its cells appear to be distinct from those of the vessel proper (Fig. 7).

The microscopic appearance of the cystic portions of the tumor is seen in Fig. 8. Each of the cysts is lined by a single layer of tall columnar epithelium with dark-staining, centrally placed, vesicular nuclei. Many of the cells are ciliated, while others show bulging of the cytoplasm into the cyst lumina. The tissue surrounding the cysts is similar to that of the nonosseous solid portions, except that the fibrous islands just described are not in evidence close to the cysts.

The metastatic nodules from omentum, parietal peritoneum, and hernial sac also had the features of osteogenic sarcoma, and were indistinguishable from comparable portions of the ovarian mass. No cyst structures were seen in the metastatic nodules.

Comment.—The morphogenesis of this tumor is questionable. That it is a true osteogenic sarcoma seems clear, but whether this was the original tumor or not is uncertain. The epithelial cells seen in Fig. 8 suggest that this tumor may have arisen from a teratoma, large portions of which were taken over by the osteogenic sarcomatous process. The fibrous islands in the soft areas of the tumor are difficult to identify; a number of observers have expressed the opinion that these represent poorly differentiated derivatives of primitive fibroblasts, and this view would tend to support the idea of a teratomatous origin of the tumor. While in hematoxylin and eosin stains there was some suggestion of secretion in these cells, stains for fat and glycogen were negative.

None of the metastases showed tissue other than osteogenic sarcoma, and this would be unusual but not impossible if the tumor were originally of teratomatous origin.

Various other origins have been suggested by a number of authors to account for the appearance of extraskeletal osteogenic sarcomas, and these varying origins are based in part on the sites at which the tumors have been found. Crane and Tremblay,[4] in a discussion of osteogenic sarcoma of the bladder, suggest that the tumor may have risen from some mesodermal structure such as the Wolffian apparatus, especially since in their case the tumor appeared to arise from the trigone. Binkley and Stewart,[5] in a general discussion of the morphogenesis of extraskeletal osteogenic sarcomas, suggest that many of these tumors are not true examples of osteogenic sarcoma, but rather are semifortuitous appearances of ossification in what is originally, for example, a fibrosarcoma. They cite as evidence of this view the fact that in many tumors little or no osteoblastic activity is seen, while osteoclasia may be prominent, and that the metastases from such tumors are almost always composed of sarcomatous elements without evidence of bone formation. In the tumor reported here osteoblastic activity is prominent, and the metastases show the same degree of active bone formation as does the primary tumor.

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2398 Sacramento Street

SPONTANEOUS RUPTURE OF THE UTERUS RESULTING FROM PLACENTA ACCRETA

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PLACENTA accreta is a relatively rare complication of pregnancy with an incidence that varies from 1 in 17,464 reported by Kaltreider in the Baltimore City Hospitals[1] to 1 in 1,956 reported by Irving and Hertig at the Boston Lying-in Hospital.[2]

Spontaneous rupture of the uterus has frequently been mentioned in the literature as a complication of placenta accreta since Alexandroff's first report in 1900.[3] In all, we were able to find a total of 10 such cases reported in the literature to the present time. We believe that the following report represents the eleventh case of spontaneous rupture of the uterus attributed to placenta accreta.

Mrs. L. M., a 33-year-old gravida ii, para i, was admitted to Huron Road Hospital April 8, 1950, with a history of a previous pregnancy in 1935 which had terminated in the delivery of a 3 pound, 14 ounce, living infant some three weeks premature. This delivery was complicated by a retained placenta necessitating manual removal. Due to excessive spotting, she returned to the hospital approximately three weeks following delivery for retained secundines, and a curettage was performed. Since that time to the present pregnancy she had not menstruated regularly and had noted frequent episodes of metrorrhagia.

At this admission it was difficult to determine the state of gestation but the patient stated that quickening had occurred about Jan. 10, 1950. The membranes had ruptured approximately one month prior to admission and one day prior to admission she complained of irregular contractions and slight bright red spotting.

Physical examination at this time revealed a well-nourished white woman showing no evidence of acute distress resting comfortably in bed. On palpation of the abdomen the fundus appeared to be three fingerbreadths above the umbilicus suggesting a seven months' pregnancy. The entire area over the fundus was rather tender to palpation with some accentuation of the pain on the left side. The fetal heart was found in the left lower quadrant, rate 144. The presenting part was high and the cervix not effaced. Pelvimetry performed at this time confirmed the diagnosis of a pregnancy of about seven months' duration. The blood pressure was 134/60; pulse 88; temp. 37° C. The admission blood count was: red blood count 4.32 million; hemoglobin 80 per cent; white count 24,000 with a differential of 90 per cent neutrophiles. A catheterized urine specimen was normal.

While in the hospital the patient continued to complain of irregular contractions and occasional "sharp stabbing" pains over the lower left abdomen. At 4:30 A.M. on April 10, 1950, the patient complained of severe contractions over the lower abdomen which woke her out of a sound sleep. She became nauseated and vomited twice. The pain then gradually increased in intensity and was not relieved by morphine sulfate, ⅙ grain. At 6 A.M. she showed evidence of acute abdominal distress. The skin was ashen in color with a profuse cold diaphoresis over the entire body. The pulse was 140, thready and weak in character. The patient was thrashing about in bed complaining of excruciating pain over the entire abdomen. On palpation of the abdomen there was generalized hyperesthesia. In spite of extreme protest by the patient the fundus was palpated, and although it appeared more tense than noted on the initial examination there was no evidence of ascent and it was apparently at the point recorded on admission. No fetal heartbeat was discernible.

The impression at this time was either spontaneous rupture of the uterus or abruptio placentae with concealed hemorrhage. Immediate treatment for shock was instituted and the patient moved to surgery, where a laparotomy was performed. When the abdomen was opened at least 1,500 c.c. of free blood, as well as multiple large clots, were found.

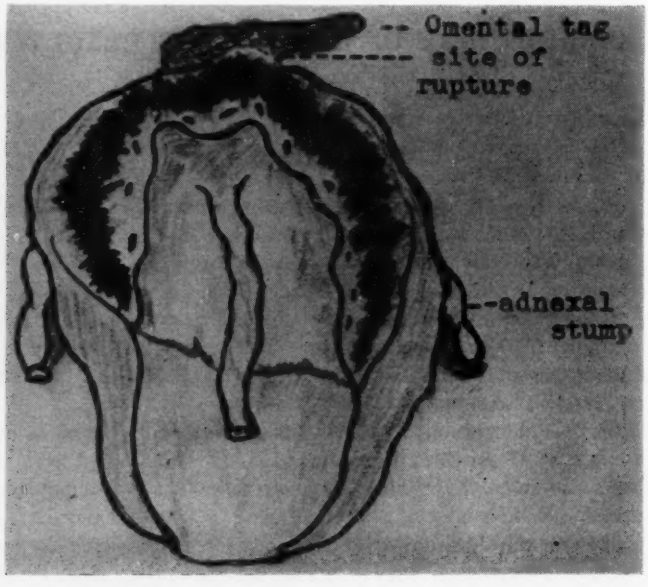


Fig. 1.—Drawing of anteroposterior view of gross specimen.

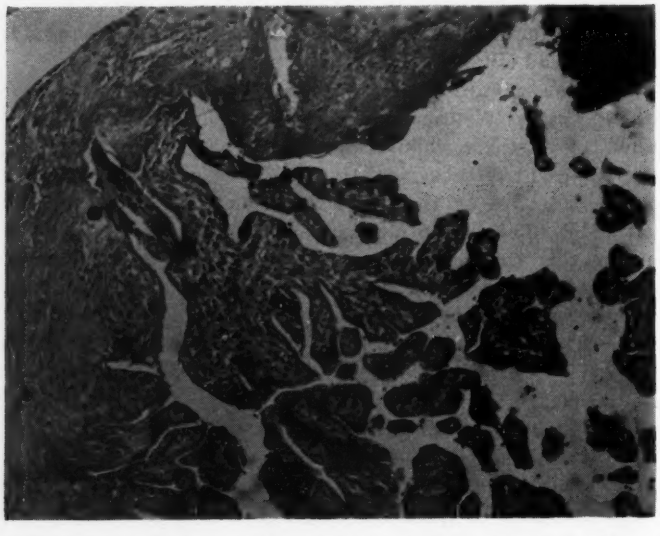
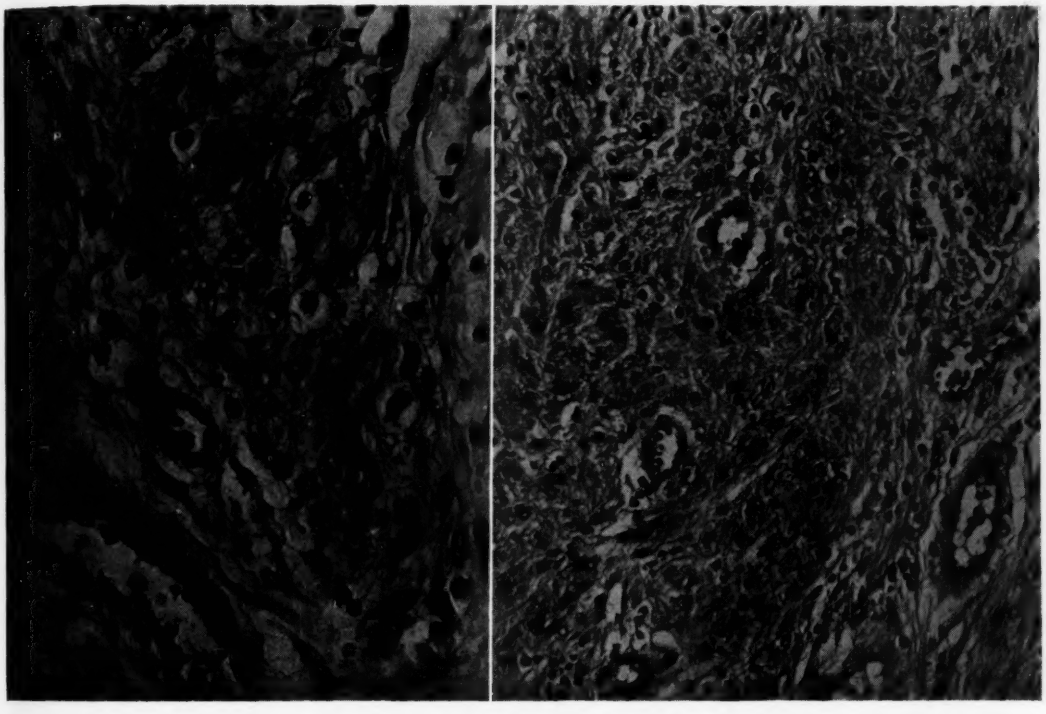


Fig. 2.—From Section 1, revealing the invasion of the uterine muscle by the chorionic villi.

The uterus appeared normal in size for a seven months' pregnancy, but the anterior wall was thinned out, somewhat darker and more doughy in consistency than normal. A midline incision was made down through the uterine wall and a living premature infant was delivered. When the uterus was withdrawn from the abdomen an omental tag was noted just above the incisional site on the anterosuperior aspect of the fundus. This was freed and at the site a small perforation was noted in the uterine wall about 1 cm. in

diameter by 3 mm. in thickness. Examination of the uterine wall at the site of rupture revealed a marked thinning of the wall with the placenta adherent to this portion. Attempts at removal of the placenta demonstrated the maternal surface to be greatly adherent to the uterine wall and apparently extending into the myometrium. In view of these findings it was elected to perform a hysterectomy which was done without event. During the operation the patient received 1,000 c.c. of whole blood and another 500 c.c. on reaching the floor. The infant died 18 hours after delivery and the postmortem examination revealed the cause of death to be atelectasis. The patient herself had an uneventful convalescence and was discharged on the ninth postoperative day.



Figs. 3 and 4.—From site of rupture.

Pathologic Examination.—"The specimen consists of uterus, cervix, placenta, and cord. The uterus weighs 430 grams and the outer surface is grayish pink in color. One area presents a small subserous fibroid 2 cm. in diameter at about the level of the uterocervical junction. At the fundus of the uterus on the anterior aspect there is a small perforation measuring 1 cm. in length by 4 mm. in thickness. On opening the uterus the placenta lies in the fundus with the remnants of the amniotic sac extending down into the region of the proximal portion of the cervical canal. Examination of the uterine wall at the point of rupture reveals a marked thinning of the wall with the placenta adherent to this portion and the entire fundal portion of the uterus. In some areas of the fundus the uterine wall is thin, measuring from 2 mm. to 1 cm. in thickness. The cord measures 25 cm. and on section the vessels show no evidence of abnormalities. The cervix is thick and short and of appearent normal size for a pregnant uterus."

Microscopic.—"Section 1 [Fig. 2] shows the endometrium markedly thickened by the mass of placental tissue with the chorionic villi small, intact and showing comparatively large vessels. The underlying myometrium shows thickening with considerable hypertrophy of the muscle cells."

"Section 2 [Figs. 3 and 4] from the site of perforation shows the myometrium markedly thinned out with considerable trophoblastic extension into the myometrium

and a few deep lying masses of placental tissue. At the margin of the perforation there is considerable necrosis and infiltration by pus cells.''

Diagnosis.—Placenta accreta, rupture of uterus.

Comment.—Although placenta accreta is mentioned frequently in the literature in the etiology of spontaneous rupture of the uterus, there have been but ten cases previously reported. Our case appears to be a well-substantiated representative of this entity, and as such is the eleventh to be reported to date.

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111 South Allen Street

A UNILATERAL OVARY WITH POLYCYSTIC DISEASE

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ALTHOUGH several series of bilateral polycystic ovaries with the Stein-Leventhal syndrome have been reported,[1, 2, 3, 4] its association with congenital absence of one adnexa has not been recorded. The clinical features of the syndrome are menstrual disorders, usually amenorrhea or oligomenorrhea, a history of sterility, a masculine type of hirsutism and, less consistently, retarded breast development and obesity. Stein, in 1929, treated this entity by ovarian wedge resection and since then the operation has been performed by him many times with the restoration of normal menstrual cycles in over 90 per cent of patients, and subsequent pregnancy in 66 per cent.[2] The degree of success is impressive and has been borne out by subsequent reports from other investigators.[1, 3, 4, 5]

Case Report.—Miss H. K. was a 33-year-old white nullipara, who was admitted to the gynecological service of Kings County Hospital on Sept. 7, 1951, complaining of hirsutism.

Her illness apparently began at the age of 17 years when she noted for the first time a growth of hair on her face, although she had had excessive hair on the extremities since childhood. The patient discerned no change in her physical contour and had no visual symptoms or voice changes until the age of 24 years when she began to gain weight, especially in the ''girdle'' region. Her menses were regular and cyclical since menarche at the age of 12½ years, until the age of 29 years, at which time they became irregular with hypomenorrhea and oligomenorrhea of two to four months' duration. Occasional intermenstrual spotting was also noted for a few months prior to admission and the patient experienced increasing right lower quadrant nonradiating pain.

Her past medical history disclosed that she was treated for syphilis at the age of 24 years and apparently cured.

Physical examination revealed a well-nourished woman with adiposity marked in the region of the abdomen and hips. One noted an essentially male habitus with a masculine distribution of hirsutism. The skin was warm but course. The breasts were full. All fingers showed clubbing. Blood pressure was 130/80 and pulse 80. On pelvic examination, inspection of the external genitals revealed a moderately hypertrophied clitoris. The uterus was small, anterior, and sinistroverted and there was a palpable ovary in the right adnexa of approximately twice normal size. Initial laboratory work showed: hemoglobin 14 Gm.; sedimentation rate 6 mm. in one hour; urinalysis normal; Kahn test 4 plus; spinal tap disclosed normal pressures and chemical examinations. Blood chemistries included: urea 31 mg. per cent; sugar 92 mg. per cent; potassium 15 mg. per cent; sodium 349 mg. per cent; cholesterol 205 mg. per cent; glucose tolerance within normal limits; 17-ketosteroid and 11-oxysteroid excretions were slightly depressed. Examination of the visual fields revealed normal confrontation and optic discs; basal metabolic rates were plus 10 per cent on three examinations; endometrial biopsy revealed a proliferative endometrium; chest plate and electrocardiogram were normal; skull plate revealed a sella turcica of normal size and outline and the pineal body was not calcified; intravenous and retrograde pyelography revealed a suggestion of a suprarenal mass which was not confirmed with perirenal air insufflation. A tentative diagnosis of a masculinizing ovarian tumor was made.

A culdoscopic examination was performed under spinal anesthesia using 20 mg. of Lucaine Hydrochloride in 3 c.c. of distilled water. The uterus appeared normal in out-

line; the right ovary was three times normal size, glistening, gray white, and smooth, and the right Fallopian tube appeared normal; the left adnexa were not visualized. At laparotomy the uterus was grossly normal and one noted a congenital absence of all the left adnexa, although a meticulous exploration of the left broad ligament was made. The right ovary measured 6 cm., was white, glistening and smooth. No ovarian wrinkling or evidence of a recently ruptured follicle or corpus luteum was noted. An ovarian wedge resection with removal of one-half of the ovarian tissue was performed. On cut surface, it was noted that the tunica albuginea was thickened and many small cysts measuring about 0.5 cm. in diameter were present. These were imbedded in the cortex and did not protrude from the surface of the ovary. The ovarian incision was approximated with a continuous atraumatic suture and hemostasis was readily secured.

Histological examination (S51-7865) revealed a thickened fibrous capsule with many small, scattered, follicular cysts in the cortex. These were lined by varying layers of granulosal cells and some by several layers of hypertrophic theca cells. Some follicles, however, lost their granulosal and theca layer and the walls showed some hyalinization. No Graafian follicles or corpora lutea were seen.

Two weeks postoperatively, an endometrial biopsy revealed a secretory phase, followed three days later by a normal menstrual period. The patient has had three successive monthly menstrual cycles. The clitoris appeared slightly smaller, but the hirsutism and masculine habitus had not materially changed at the time of the three-month postoperative examination.

Comment.—The etiology and pathogenesis of polycystic ovarian disease are not well understood and there has been consistent failure to demonstrate hormonal imbalance by available endocrinological studies. This would tend to support the thesis of an intrinsic mechanical ovarian factor, congenital or inflammatory in origin, resulting in the thickened capsule and an increased intraovarian pressure. It has been postulated that a distortion of the spiral arteries in the ovarian hilum is due to pressure from the multiple cysts and perpetuates this condition by causing further anoxia to the ovarian stroma and follicles. All patients with menstrual disorders, hirsutism, sterility, and obesity should be kept under close observation and studied by repeated hormonal assays to rule out specific endocrine disorders, endometrial biopsies to establish the presence of ovulation, culdoscopy and gynecography if available. This lesion is infrequently mentioned in discussions of masculinizing tumors of the female and should be thought of more often in differential diagnosis. The syndrome of large pale ovaries may be differentiated from the adrenogenital syndrome mainly by the presence of very high 17-ketosteroid excretions in the latter condition, 2 to 10 times normal or more. Whereas the adrenogenital syndrome is primarily a genital disturbance, Cushing's disease is metabolic, so that in addition to the triad of hirsutism, amenorrhea, and obesity, one notes hypertension, decreased glucose tolerance, and muscular fatigue. Pyelograms showing distorted calyces with rotated and displaced kidneys suggest adrenal tumors. Usually polycystic ovarian disease has a gradual onset whereas in tumors of the adrenal cortex or the arrhenoblastoma there is a sudden appearance of hirsutism in a previously nonhirsute woman. Another interesting, perhaps related, observation was made by Dockerty[6] who studied 36 patients under 40 years of age with adenocarcinoma of the corpus uteri and noted 20 per cent in whom four or more of the cardinal features of this entity were present.

The end results in this patient parallel the findings of others and, whatever the pathogenesis may be, partial resection is usually followed by restoration of normal menses and reproductive function. This case may also serve as further proof that one ovary can assume all the functions exercised by both ovaries even after its resection and demonstrates the value of conservation of ovarian tissue in women of the childbearing period.

Summary

1. An additional case of polycystic ovarian disease is reported because of its unusual association with congential absence of the adnexa on one side.

2. This patient, treated by ovarian wedge resection, has begun to menstruate normally and subsequent endometrial biopsies taken at one and two months postoperatively have revealed a normal secretory endometrium and thereby give presumptive evidence of ovulation.

I wish to acknowledge with thanks the helpful suggestions of Dr. Charles W. Mueller Director of the Service.

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706 Eastern Parkway

RETROPERITONEAL HEMATOMA DURING PREGNANCY

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MASSIVE retroperitoneal hematoma is a rare and usually fatal complication of pregnancy. There are only four reported recoveries from this grave complication. Our case represents what we believe to be the fifth recorded survival.

M. J. (No. 170008) is a 34-year-old Mexican woman who had eight previous pregnancies, one of which resulted in a stillbirth. Her present pregnancy was calculated to be at term on April 1, 1948. The pregnancy was an uneventful twin gestation until March 10, on which date she delivered twin female infants spontaneously. Her labor was complicated by slight vaginal bleeding due to marginal separation of the placenta, for which she received 500 c.c. of blood by transfusion.

In the morning of the first postpartum day, she began to complain of right lower quadrant pain. This pain was interpreted by a Spanish-speaking physician as "after pains." At 7 P.M. on March 12, thirty-six hours after the onset of the pain, she was found in deep shock.

Preparations were immediately made for an exploratory laparotomy, and for massive transfusions through two "cut downs" of unmatched type O Rh-negative blood. The abdomen was opened through a midline incision which was later extended to the costal margin. Throughout the operation, despite 3,500 c.c. of whole blood, 1,200 c.c. of plasma, and 3,000 c.c. of glucose and saline, she was in shock. For only brief moments the blood pressure could be obtained and the pulse felt. When the skin incision was closed at 11 P.M. although her blood pressure was 110/60, her condition was critical.

The operation revealed a huge retroperitoneal hematoma extending from the right broad ligament to the diaphragm, and from the midline to a point lateral to the ascending colon. It was estimated that this contained 3,500 c.c. of blood and clots, and that the total blood loss exceeded 5,000 c.c.

Believing that a rupture of the uteroovarian veins caused the hematoma, a subtotal hysterectomy was rapidly performed. Despite this procedure, the hematoma continued to enlarge. When the posterior peritoneum was opened, blood and clots were removed from the retroperitoneal space. The hemorrhage seemed to be coming from the region of the right kidney pelvis; consequently the kidney was removed. However, following this, the hemorrhage was still not controlled. Further clearing of blood and clots from the space demonstrated that most of the blood seemed to be coming from some of the vessels near the midline. The inferior vena cava was ligated with chromic catgut in several places beginning near its origin and ending at a point just below the termination of the left renal vein. Also, several lumbar veins on the right and the right sympathetic chain along this portion of vena cava were ligated. This latter procedure of ligating the vena cava and the lumbar veins on the right seemed to control the hemorrhage.

When the patient was placed in bed, her blood pressure could not be registered. Throughout the night, she received more blood, oxygen, and penicillin. An indwelling catheter was placed at 11 P.M. No measurable amount of urine was excreted from that time until 8 A.M. on March 13. At that hour, the blood pressure could not be measured, and the heart rate was 180. During that day she received an additional 1,000 c.c. of blood, and enough other fluids to keep the "cut down" working. At 11 A.M. the blood pressure was 75/50; at 2 P.M., 86/55;

and she excreted 400 c.c. of urine since 8 A.M. At 6 P.M. the blood pressure was 98/60. She was alert and resting. Levine suction was started prophylactically. This latter was used intermittently during the next several days.

On March 14, she continued to improve. Her blood pressure was 110/70, pulse 100, and temperature was 38° C. For the previous 12 hours, the urinary output had been 400 c.c.

On March 15, the blood pressure was again 110/70. The urinary output for the previous 24 hours was 1,110 c.c. The use of the "cut down" was discontinued.

March 16 she developed diarrhea which was promptly controlled by paregoric and bismuth.

On March 18, she was permitted to get up. A thrombophlebitis of the right leg began on March 20. This was treated by the administration of three long-acting spinal anesthetics consisting of Pontocaine (5 mg.) weighted with 10 per cent glucose with Adrenalin added. On the following day, the dosage was increased to 8 mg. of Pontocaine. The spinal anesthetics were continued until March 23, when all signs of thrombophlebitis had disappeared.

On March 25, both legs were markedly edematous, but no signs of phlebitis were present. She was finally discharged on April 1, asymptomatic except for pitting edema of the legs.

Her hemoglobin on admission was 13.9 Gm., and on discharge 9.9 Gm. She was type O, Rh positive.

On April 19 she was seen in the Clinic for her postoperative examination which showed marked edema of the right leg, and some tenderness in the right adnexa. On June 18 this edema had completely disappeared. The results of an intravenous pyelogram taken on July 7 demonstrated a normal left kidney.

Comment:—In the 150 years prior to 1904, J. Whitridge Williams tabulated thirty-three cases of severe puerperal hematomas, of which fifteen were retroperitoneal. All of the latter were found on postmortem examination. Since 1904, ten cases of severe retroperitoneal hematoma have been described by various authors. Of these ten, only four patients have survived.

In the group reported prior to 1904, little information is available as to the origin of the bleeding. However, since that time, in the cases that came to autopsy, a significant portion of them have evidence of some antecedent vascular disease either in the form of aneurysmal dilatations of various vessels (Potocki, Wilson, Low, Danforth) or in the form of "thin walled vessels" (Scrivener, Low).

The existence of vascular disease does not alone account for the hemorrhage. Physical stress occurred prior to the onset of symptoms in many of the cases. This was the stress of labor in many cases, and in others it was the stress of defecation or coitus. Hypertensive toxemia was present occasionally to add to the stress borne by the vascular system.

Another factor which may be present in some of the cases, but which has not been subject to evaluation, is the possible presence of conditions which may interfere with the clotting mechanism of the blood. This was discussed in considerable detail by Kistner and Garber.

After the accident has once occurred, the treatment of the patient is of paramount importance. Adequate transfusion of whole blood begun immediately and pursued vigorously is of greatest importance. Those patients who recovered received more than 1 L. of blood. Our patient received 3,500 c.c. of blood, 1,200 c.c. of plasma, and 3,000 c.c. of glucose and saline during the operative procedure. During the first postoperative day, she received an additional 1,000 c.c. of blood. In other cases reported (Scrivener, Kistner and Garber) massive transfusion was likewise employed.

In four of the five reported survivals, a surgical operation was performed in an attempt to control the bleeding. In two of the cases the hematoma was not disturbed, while in three the hematoma was attached surgically either by packing or by ligation of bleeding vessels. The latter was effected by nephrectomy, packing, hysterectomy, or by direct ligation of bleeding vessels. It appears that an attempt to control the bleeding by actual operation upon these gravely ill and shocked persons may improve the prognosis of the patient, especially if adequate transfusion is employed.

Summary

A survival from massive retroperitoneal bleeding is reported. The condition seems to arise in individuals who are placed under some stressful condition and who, at the same time, may have a predisposing vascular disease.

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1304 CHESTER AVENUE

POSTABORTAL SEPSIS TREATED WITH SURGERY AND ANTIBIOTIC THERAPY*

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THE patient, a 21-year-old unmarried Negro woman, was first seen in the emergency room of Albert Merritt Billings Hospital on March 20, 1949. She complained of pain in the left lower quadrant of three days' duration. Examination revealed a profuse vaginal discharge and gram stain of this discharge was said to contain many gram-negative intracellular and extracellular diplococci. The patient was acutely ill, with a temperature of 39° C., and she was admitted to Billings Hospital on the Employees Health Service, where treatment with penicillin was instituted. Her condition failed to improve, and on the second hospital day (March 22) distention and nausea developed but she did not vomit. The conjunctival sac revealed an icteric change. On this same date she admitted that an abortion was induced 15 days before (13 days before admission to the hospital). By history the pregnancy was of approximately six weeks' duration. She was then placed on a peritonitis regimen and was fed parenterally. Prior to the revelation of the abortion x-ray films of the abdomen showed marked distention of the ascending and transverse colon. By means of a barium enema an apparent obstruction of the colon was noted at the splenic flexure and moreover a distended loop of transverse colon was displaced down into the pelvic inlet. A diagnosis of pelvic peritonitis was made and the obstetrical and gynecological service was asked to accept the patient. The patient was transferred to The Chicago Lying-in Hospital on her third hospital day.

On admission to Chicago Lying-in, cervical and urethral cultures were taken, and an intrauterine culture was also taken. The cervical and urethral cultures were negative for gonococci and other specific organisms, as *Clostridium welchii*. The intrauterine culture revealed only *Escherichia coli*.

Gastric suction was started immediately after admission to this hospital. Hydration was maintained with parenteral fluids, pooled plasma, and whole blood transfusions. The white blood count was 29,700 on March 21, fell to 13,100 on the following day, and then gradually rose to a peak of 38,900 on March 27. Differential count showed 82 to 88 per cent polymorphonuclear leukocytes with a shift to the left. Blood chemistry on March 22 revealed nonprotein nitrogen of 31 mg. per cent, total protein of 7.2 Gm. per cent, albumin of 3.69 Gm. per cent, and a direct serum bilirubin of 3.0. On March 27, nonprotein nitrogen was 11 mg. per cent, total protein 5.8 Gm. per cent, albumin 1.7 Gm. per cent, globulin 4.1 Gm. per cent, serum chlorides expressed as sodium chloride 550, and indirect serum bilirubin 4.8.

The patient's condition gradually deteriorated from March 22 until March 27, with increasing distention, a plateau temperature of about 39° C., with a pulse rate above 120. Attempts at decompression with a Miller-Abbott tube failed. On March 27 it was elected to decompress by means of colostomy. When the abdomen was opened, numerous plaques of dry exudate were found in the visceral peritoneum, and an adhesive band was found obstructing the transverse colon near the splenic flexure. Both the small and large bowels were involved by extensive dry adhesions. The entire peritoneal cavity was unusually dry. The adhesions of the transverse colon over the pelvic inlet were broken and the rest of the bowel

*Supported in part by The Chicago Lying-in Hospital Fiftieth Anniversary Fund for Research on Puerperal Infection.

freed from the duodenum to the pelvic inlet. Although the patient's condition was extremely serious, this procedure seemed justified to learn how these peculiar reactions in peritonitis had occurred after antibiotic therapy.

Behind the uterus and on the left side was a large localized mass typical of a pelvic abscess. This mass had been identified on vaginal examination before surgery. It was elected to leave it intact until the obstructed areas had been freed.

A loop of transverse colon was mobilized and brought out through the incision. It was anchored in place and fixed by a glass rod through the mesentery. Just before closing the parietal peritoneum 400,000 units of penicillin, 2 Gm. of streptomycin, and 5 Gm. of sulfathiazole were instilled into the peritoneal cavity.

After the laparotomy the patient was placed in the lithotomy position and a cul-de-sac puncture and incision were done. A few hundred milliliters of pus were obtained. A rubber drain was fixed in the abscess cavity. The primary intestinal obstruction site was at the splenic flexure and not associated with the pelvic abscess. Cultures of the pus obtained by cul-de-sac puncture revealed an anaerobic, nonhemolytic streptococcus and bacteroides. The organism was typical of *Bacterium melaninogenicum* but it was never isolated or culturally identified.

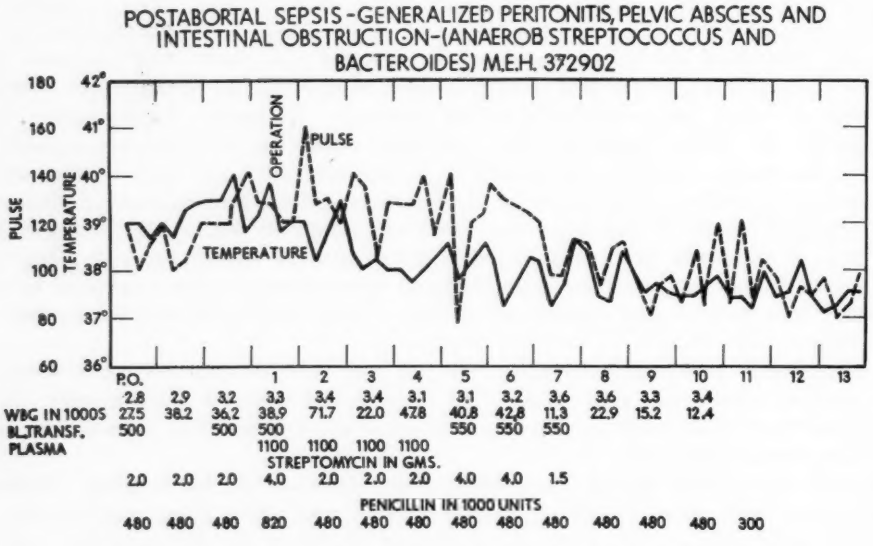

Fig. 1.

The patient's course postoperatively continued very stormy. On March 28, the second postoperative day, her white blood count increased to 71,700 with still a marked shift to the left. The count remained above 40,000 until the seventh postoperative day, when it dropped to 11,300, and it remained generally under 15,000 for the rest of the hospital stay. The hematocrit varied between 31 per cent and 36 per cent. On the fourth postoperative day, the nonprotein nitrogen was 19 mg. per cent, serum chlorides expressed as chloride were 94.6, serum pH was 7.39, and carbon dioxide was 28.3. The following day, nonprotein nitrogen was 24 mg. per cent, serum chloride was 91.6, and carbon dioxide was 28.7.

The patient was treated symptomatically with fluids, blood transfusions, and vitamins. She received 480,000 units of penicillin and 2 Gm. of streptomycin daily until the eleventh postoperative day. Her condition improved gradually and on the seventh postoperative day gastric suction was discontinued. Clear liquid diet was introduced and increased gradually.

On the twenty-eighth postoperative day the patient's condition was much improved and at this time she was transferred back to Albert Merritt Billings Hospital where, on the

thirty-first postoperative day closure of the colostomy was done. Her postoperative course following that procedure was relatively uneventful. She was last seen in the Out-Patient Clinic on the seventh day following her discharge from the hospital. There was only a minimum of inflammatory reaction remaining. The bowel function was stated to be normal. The general appearance of the patient was excellent for this early postoperative visit. The graph indicates the general course of the patient.

Summary and Conclusions

A case of postabortal sepsis involving bowel obstruction treated by surgery and adequate antibiotic therapy has been presented. While surgical intervention and colostomy are not recommended routinely such steps may become necessary to effect decompression. Obviously these patients must be selected most carefully. It is emphasized that the gross pathological picture of peritonitis may be altered to a striking degree. In this case, from only two sites in the abdominal cavity were positive cultures obtained even though there had been recently a generalized peritonitis.

This type of case would have been fatal most certainly prior to the era of antibiotic therapy.

NOTES ON THE 8 AND 24 HOUR FRANK-BERMAN PREGNANCY TEST

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THE Frank-Berman pregnancy test, first described in 1941, is the first successful pregnancy test using rats with results in 8 and 24 hours. At this time a review of the test based on experience with many thousands of tests, of the precautions to be followed, and a general discussion of the role of a pregnancy test are indicated. The great number of inquiries received from physicians for help in interpretation of tests plus the great number of incorrect results that physicians have received from laboratories using varying tests and techniques have prompted this review.

Technique of Test.—

1. The test animals required are two immature female rats, weight 50 grams (weight range, 45 to 60 grams).

2. Two subcutaneous injections of test urine are made, a 5 ml. dose at each injection.

3. The animals are sacrificed next morning with illuminating gas, the ovaries dissected out and read grossly with the naked eye.

The urine to be injected is first centrifuged to bring down extraneous matter—crystals, urates. white blood cells, epithelial cells, etc.—which are not necessary for the test and the clear supernatant urine which contains the hormone is used. The animals are given two subcutaneous injections, 5 ml. at each injection, one injection being given in the morning, the second injection in the afternoon, with a minimum time interval of 4 hours between injections. The injection needle is inserted under the loose skin of the rat, the needle being pointed toward the tail of the animal. After the injection, massage the skin downward at the injection site to help spread the injected urine over a larger surface.

The following morning, the animals are killed with illuminating gas. Keep the animals in the lethal chamber with gas entering the chamber until they are dead, not just gasping. The ovaries are then dissected out via the abdominal route. The ovaries are read grossly with the naked eye. It will facilitate matters to place the dissected ovaries on a piece of slightly moistened gauze and read immediately. A negative ovary is small, pale, and creamy in color or slightly pinkish, the surface of the ovary showing minute colorless follicles. A positive ovary is usually, but not always, enlarged, and is entirely reddened or may have many distinct red spots on it.

In the 24 hour period, luteinization in the ovary does not occur. It takes 48 hours for the ovary to become luteinized. It is absolutely necessary to use illuminating gas to sacrifice the animals since the anoxia following exposure to carbon monoxide affects the capillaries of the ovaries, giving the characteristic reddened effect to positive ovaries. Microscopic sections of the 24 hour test ovary show that the characteristic hyperemic zone is due to hyperplasia of the theca interna cells with marked multiplication and dilatation of the ingrowing capillaries. It is apparently the chorionic gonadotropic hormone which affects the vascular system of the ovary and with the use of illuminating gas the typical carbon monoxide effect on the ovary is therefore produced.

Since 3.5 per cent of the rats are refractory, the test must be done on two rats. Occasionally, in a rat one ovary will be negative and the other ovary positive. This is a positive pregnancy test. The test, if performed as described and all precautions followed, is 100 per cent accurate.

Precautions to Be Followed.—

There are certain precautions which must be observed by the patient or the test may be valueless. The instructions to be given patients for the test are:

1. Take no medication—hormones, Prostigmine, antihistamines, laxatives, sulfonamides, quinine, ergot—for 96 hours prior to test. (These substances are toxic and will kill the test animals. Toxic urines cannot be detoxified.)

2. Drink no alcoholic beverages for 24 hours prior to test. (Excreted alcohol is toxic to the test animal.)

3. Save first urine on arising, put into refrigerator immediately. Keep in refrigerator until brought to laboratory. (Do not restrict fluids for the purpose of concentrating the urine. The concentrated urine will either kill the animals or make it difficult to read the ovaries. There is sufficient concentration in the overnight normal concentration. It is unwise to use any random specimen of urine. The patient may have had a diuretic such as coffee, tea, cola, etc., which will induce urination with a subsequent dilute specimen, or the patient may be a low hormone excreter and the hormone excreted in a random specimen may therefore be too little to be picked up by the animals. It is necessary to keep urine refrigerated since the gonadotropic hormone deteriorates at room temperature.)

4. Bring a 2 ounce specimen to the laboratory in the morning.

The urine specimens should be kept refrigerated at all times. Before injecting the urine it should be allowed to stand at room temperature for about 20 minutes so as not to shock the animals. Urine can be kept in the refrigerator for several weeks without deterioration of the hormone.

Hydatid Mole and Chorionepithelioma.—

In cases of suspected chorionepithelioma or hydatid mole, a urine titration pregnancy test is necessary as a diagnostic procedure. A normal pregnancy may give a positive reaction with as little as 0.1 ml. urine. Therefore, positive results below this level are indicative of a hydatid mole or chorionepithelioma since in both these conditions there is a great excess of chorionic gonadotropic hormone excreted. In suspected cases, a routine pregnancy test with a 10 ml. urine dose is done. If this is positive, proceed with the following dose ranges of urine: 5 ml., 1 ml., 0.1 ml., 0.05 ml. In making up the dilutions, prepare them so that the total amount injected into each rat is 10 ml.:

Dilution A, 5 ml. dose—15 ml. urine + 15 ml. distilled water
Dilution B, 1 ml. dose—4 ml. urine + 36 ml. distilled water
Dilution C, 0.1 ml. dose—4 ml. from Dilution B + 36 ml. distilled water
Dilution D, 0.05 ml. dose—15 ml. from Dilution C + 15 ml. distilled water

If a positive reaction is obtained with the 0.05 ml. dose, further dilutions are necessary. Proceed with 0.025 ml. dose, 0.0125 ml. dose, 0.00625 ml. dose, etc. Extreme care must be taken to wash the syringe and needle very carefully between injections of different dose ranges to prevent the carry-over from one dose range to another.

Repeated pregnancy tests must be done in all cases of hydatid mole until the pregnancy test is negative. If after the removal of the hydatid mole, repeated pregnancy tests are negative followed by a positive pregnancy test or if the pregnancy tests remain positive, the possibility of the transformation of the mole to chorionepithelioma must be seriously considered.

Ectopic Pregnancy and Other Conditions.—

In cases of suspected ectopic pregnancy, the pregnancy test may be negative or positive. The test will be positive only if the chorionic villi are attached. Therefore, a negative pregnancy test does not signify the absence of an ectopic pregnancy.

In cases of abortion, positive pregnancy tests will be obtained if fragments of placenta are retained or if fragments of chorionic villi are still retained and attached.

Use of Blood Serum.—

The Frank-Berman pregnancy test may also be done with blood serum. It is a simpler procedure for the patient to bring in a urine specimen than to be subjected to blood withdrawal. However, in the following cases it is necessary to do the test with serum:

1. If the patient has cystitis, the urine will kill the animals.
2. If the patient is under medication that will prove toxic to the animals and the physician needs an immediate pregnancy test.
3. If the patient is bleeding, urine may prove toxic.
4. If the patient is diabetic, the urine specimen may be very dilute because of the associated polyuria. In diabetes, it is therefore essential to do the pregnancy test with serum.

The serum is administered by subcutaneous injection, 1 ml. in the morning and 1 ml. in the afternoon, making a total of 2 ml. serum for each rat.

General Comments.—

As reported in our first publication, results can also be obtained in 8 hours. However, since a negative result in 8 hours cannot be considered a true negative unless confirmed by the 24 hour test, the value of the 8 hour test is limited. Another factor to be considered is the time element involved for laboratory personnel. Since urine specimens will arrive at the laboratory at varying time intervals, it is impractical to start tests at varying times and then report back to the laboratory at varying time intervals to kill and autopsy the animals.

The 24 hour test has time latitudes that will fit into the ordinary working day of a laboratory. The animals ideally can be given the first injection at 10 to 11 A.M. and the second injection at 4 to 4:30 P.M. If urine arrives later, injections can be given at 1:00 P.M. and 5:00 P.M. If a urine specimen arrives later in the afternoon and laboratory personnel are available to report back to the laboratory in the evening, animals can be injected at 6:00 P.M. and again at 10:00 P.M. All animals are sacrificed the next morning at 8:00 to 8:30 A.M. This therefore makes the 24 hour pregnancy test a 16 to 24 hour test. Time ranges below 16 hours are not reliable and dose ranges below 10 ml. are also unreliable. Since the levels of hormone excretion differ from patient to patient, 10 ml. was adopted as the correct dose range to cover all types of excreters.

It is usual for a woman to suspect pregnancy when menstruation is delayed. It is therefore very difficult to determine the earliest time at which pregnancy can be detected. The earliest pregnancy we were able to pick up was a ten-day pregnancy, counting cycle day ten as the first day of pregnancy. This case was picked up in the course of research on control cases—normal menstruating women, cases of primary and secondary amenorrhea, menopause cases, etc. Our diagnosis of pregnancy, which amazed the patient who had not yet had a chance to "miss" menses to suspect pregnancy, was confirmed.

It should be pointed out also that there are more cases of early abortion than are suspected in so-called "sterility" cases. We had many cases that we could follow very closely where positive pregnancy tests were obtained followed by "menses." Immediate examination of these women was made and whatever was found on the examining glove finger was sectioned. In all cases, chorionic tissue was found on section.

Before attempting to perform the pregnancy test, it is absolutely imperative that many tests with known negative and positive urines be performed to learn to read the ovaries correctly.

Role of the Pregnancy Test.—

The pregnancy test is used to diagnose pregnancy, the presence of retained fragments of placenta or chorionic tissue, hydatidiform mole, and chorionepithelioma in the male as well as the female. The pregnancy test will not predict abortion, will not indicate the progress of the pregnancy, will not indicate whether the fetus is dead or alive, will not definitely

establish an ectopic pregnancy, nor will it tell the ovulation time. The physician has a definite role in the interpretation of the pregnancy test in conjunction with the symptoms of the patient.

Summary and Conclusions

1. The Frank-Berman 24 hour pregnancy test, which consists of injecting two immature rats with 10 ml. urine, is described.

2. The Frank-Berman pregnancy test is used to diagnose pregnancy, hydatidiform mole, chorionepithelioma, and the presence of retained products of conception in aborting patients.

3. If all conditions described for the test are followed, the test is 100 per cent accurate.

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BILATERAL ECTOPIC GESTATION

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THIS case is reported because of the rarity of the condition and because of several interesting features which it presents. Abrams and Kantor,[1] in 1948, reported the incidence of bilateral ectopic gestation to be 1:1,580 ectopic pregnancies. Stewart[2] in 1950, in his report of a case, reviewed the world literature and reported the incidence to be 1:725 ectopic pregnancies. In all, 212 cases have been reported and have been divided into three groups. Group I consists of seven cases reported prior to 1890 which are mainly of historical interest. Group II contains 139 acceptable cases, consisting of both coexisting and simultaneous bilateral ectopic pregnancies. Group III consists of 66 cases which are not acceptable because of a lack of fulfillment of the accepted criteria. An additional case of multiple ectopic gestation was reported by Philips[3] in 1950. Fishback[4] in 1939 pointed out that the embryo or chorionic villi must be present bilaterally in order to establish a diagnosis of bilateral ectopic gestation. The authors feel that the following case fulfills Fishback's criteria and would probably fit into Stewart's classification, Group II. To the best of our knowledge, it is the one hundred forty-second reported case.

Case Report.—G. S., a 32-year-old Negro woman, para iv, gravida iv, was admitted to the Gynecological Service of Cumberland Hospital on Sept. 15, 1951, complaining of lower abdominal pain of three days' duration. The onset of the present illness occurred on the afternoon of Sept. 12, 1951, three days prior to admission, with sudden, sharp lower abdominal pain followed by syncope. Following the initial attack, the patient exhibited vaginal spotting and experienced severe nausea and vomiting. The abdominal pain, knifelike in character and continuous, and the vaginal spotting increased steadily in intensity and continued to the time of admission. The patient gave no history of missed or abnormal menses. Her last menstrual period was on September 5 for four days and the prior menstrual period on August 5 for four days.

The family history was noncontributory. Her past history was essentially negative, as she had had no previous surgical procedures or serious illnesses. The patient had had four pregnancies, all resulting in delivery of normal, full-term children without complication or difficulty. The last delivery was seven and one-half years prior to the present admission. Her menses had always been regular, occurring every thirty days for four days without discomfort. Venereal infection was denied, and there was no history of pelvic inflammatory disease.

Physical examination on admission revealed a well-developed, well-nourished Negro woman in acute distress. The skin was cold and clammy. Oral temperature was 100° F. Pulse was 110, rapid and thready. Respirations 32, were rapid. Blood pressure on admission was 90/50. The heart and lungs were negative except for a tachycardia. Colostrum could be expressed from both breasts. The abdomen was distended and felt doughy on palpation. There was tenderness over both lower quadrants, but more marked on the left, with moderate rigidity over the lower abdomen. Rebound tenderness was elicited over the entire lower abdomen.

Pelvic examination revealed a parous introitus. There were no external signs of infection or evidence of vaginal bleeding. The vaginal mucosa was extremely pale. The cervix was in the anterior position, gaping, lacerated, and exquisitely tender on motion. There were fullness and bulging of the right fornix. The left fornix could not be palpated

adequately because of abdominal resistance and exquisite tenderness and pain. There was an impression of a mass in the right adnexal region but because of the patient's pain and voluntary rigidity, no further pelvic organs could be palpated. A clinical diagnosis of hemoperitoneum due to ruptured ectopic gestation was made at this time.

Laboratory tests revealed the following: hemoglobin, 7 Gm. per 100 c.c.; erythrocyte count, 2.18 million; white cell count, 27,000 with a differential of 87 per cent ploymorphonuclear cells, 8 per cent lymphocytes, and 5 per cent monocytes. There was slight basophilic stippling of the erythroctyes. Sedimentation rate was 18 mm. in 40 minutes (Cutler method). Urinalysis showed one plus sugar (following an intravenous injection of glucose), one plus protein, and 3 to 4 white blood cells per high-power field. Blood grouping was A, Rh positive.

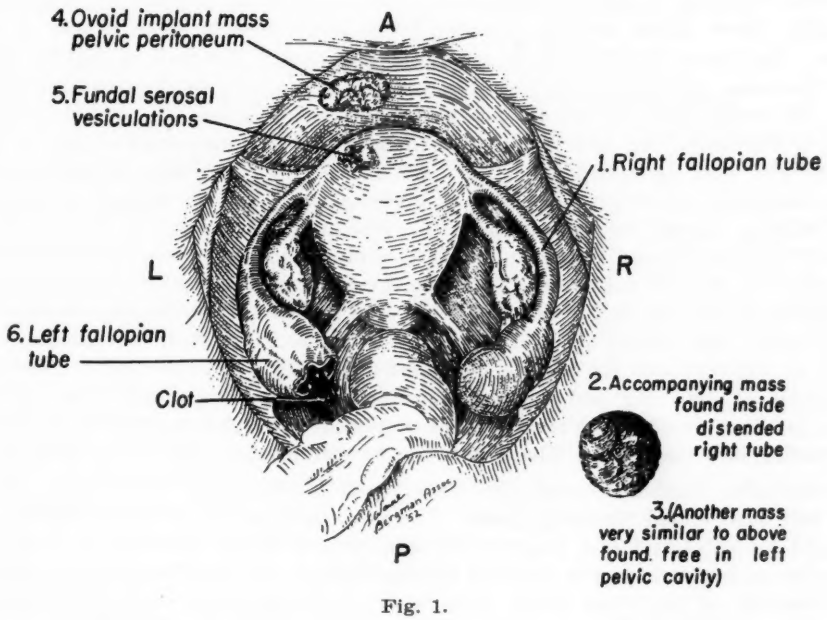

Fig. 1.

Immediately upon admission, antishock therapy was instituted. An intravenous infusion of 5 per cent glucose in saline was started while whole blood was being crossmatched. The patient then received 500 c.c. whole blood on the ward. A laparotomy was performed under general anesthesia. The abdomen was opened in layers through a left paramedian incision. Approximately 1,500 c.c. of fresh blood were found in the peritoneal cavity. Exploration revealed a free mass, grayish white in color, firm, irregular, just below the fimbriated end of the left tube. Blood was oozing freely from the osteum of the fimbria from which a blood clot also protruded. A left salpingectomy with cornual resection was performed, and the active bleeding was controlled. Further exploration at this time revealed a nodular dilatation of the right tube. An incision was made in the tube and a mass was extruded similar to the free mass found in the peritoneal cavity. A right salpingectomy with cornual resection was then performed. Further exploration revealed a rough, red, vesiculated area on the fundus of the uterus of which a biopsy was taken. On the parietal peritoneum of the pelvis, to the left of the symphysis, was found an olive-colored mass, approximately 3 cm. in diameter. This, too, was excised. The abdomen was then closed in layers. The patient's condition following this procedure was good, as she had received 1000 c.c. of whole blood during the operation.

The postoperative course of the patient was excellent. Skin clips were removed on the fourth postoperative day and she was discharged to the outpatient department for

follow-up on the tenth postoperative day. She has been seen periodically for the past three months, and her course has been excellent.

Pathological Report (by Dr. Silik H. Polayes).—

Macroscopic.—The specimen consists of (1) a right Fallopian tube with (2) an accompanying irregular mass about 3 cm. in greatest diameter, i.e., right tubal content; (3) another mass about 2 cm. in greatest dimension, i.e., the free structure removed from the left pelvic cavity; (4) an ovoid mass about 2.5 cm. in diameter, i.e., the implant on the pelvic peritoneum; (5) a soft small mass, 5 mm. in diameter, i.e., biopsy from the fundus; and (6) a left Fallopian tube.

The right tube (1), about 10 cm. long, was received sectioned, and presents in its midisthmic portion a dark gray, firm, granular, solid structure attached to its mucosa and measuring about 5 cm. in greatest dimension. This is continuous with a saclike, softer, pink tissue which projects into the lumen and measures about 4 mm. in greatest diameter. The lining of the tube is thickened and gray. The wall is slightly thickened and on the serosa presents slightly raised red areas, especially in the portion opposite the mass in the lumen just described. The accompanying structure (2), i.e., the right tubal content, is bilobed: one lobe entirely irregular in shape, measuring 1 cm. in greatest dimension and pink in color; the other lobe, more ovoid in shape, measuring 2 cm. in greatest diameter, yellow-gray in color and edematous. Section showed a homogeneous smooth surface, except for lobulations. The free mass (3) found in the pelvic cavity measures 2 cm. in greatest diameter and is discrete, solid, firm, and of yellow-gray color. Section shows a smooth cut surface. The peritoneal implant (4) is an ovoid, soft hemorrhagic structure, 2.5 cm. in greatest diameter, and presents a central degenerated area of gray-red color. The biopsy of the fundus (5) is 5 mm. in greatest dimension. One portion of it is muscular and the other is composed of smooth, pink, soft tissue. The left tube (6) is about 12 cm. long and contains a nipplelike hemorrhagic cylindrical mass about 3 mm. in greatest dimension in the proximal portion of the isthmus, attached to the mucosa and projecting into the lumen. The fimbria are hemorrhagic, as are also portions of serosa.

Microscopic.—Section through the mass found in the right tubal lumen (1) shows calcified and degenerated placental tissue. The continuous saclike structure contains similar degenerated placental villi and degenerated membranous lining identified as amnion. The serosal areas of hemorrhage are decidual reactions which are hypervascularized and hemorrhagic. Section of the right tubal content (2) is composed of folds of tubal mucosa (fimbria) to which is attached an irregular hyalinized, fibrous structure in areas enclosing fat and collections of lymphocytes and covered by a lining of cuboidal and low columnar epithelium. The free mass found in the pelvic cavity (3) shows degenerated calcified placental villi. The peritoneal implant (4) is an organizing fresh hematoma containing degenerating placental villi. The fundal biopsy (5) is composed of myometrium and decidual reaction in the serosa. Section through the cylindrical projecting mass of the left tube (6) shows viable placental villi growing from the implantation in the mucosa where a mild decidual reaction is observed. The decidual reaction is also demonstrable in the serosa where there are occasional groups of fetal cells.

Diagnosis.—A pathological diagnosis was made of old degenerated right tubal gestation with pelvic lithopedion and recent left tubal gestation with abortion and hemorrhage including chorionic villi in both Fallopian tubes in addition to a pelvic decidual reaction.

Comment.—The above pathological findings fulfill Fishback's criteria. The placental villi found on the parietal peritoneum lend evidence to the presumption that there was a last effort of the aborted gestation to implant itself.

Again, as has been true in other cases of this type reported in the literature, the diagnosis of bilateral ectopic gestation was made at operation. Since there are no particular characteristic signs or symptoms peculiar to this entity other than those referable to a unilateral ectopic gestation, we believe it is almost invariably a diagnosis made at operation.

Bilateral salpingectomy was performed as a procedure of choice rather than a more extensive procedure because of the patient's poor condition due to the shock caused by the intraperitoneal hemorrhage. This case also demonstrates the importance of examining both adnexa in a laparotomy for an ectopic gestation.

Summary

1. A case of bilateral ectopic gestation is presented.

2. Abortion of the left tubal gestation took place with resultant intra-abdominal hemorrhage.

3. The diagnosis of bilateral ectopic gestation is an operative one.

4. It is emphasized that both adnexa must be examined when a laparotomy is performed for unilateral tubal gestation or other adnexal pathology.

5. The simplest operative procedure should be chosen in shocked patients.

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SQUAMOUS-CELL CARCINOMA DEVELOPING FROM A MARSUPIALIZED DERMOID OF THE OVARY

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CASE No. 147645. C. H., a 67-year-old white woman, entered the Swedish Covenant Hospital on Jan. 12, 1947. Two days prior to admission she had a sudden chill, which lasted for several hours, and at the same time a rather severe abdominal pain developed. There had been no bowel movement for 24 hours.

The past history was irrelevant, except that the patient was under observation for gall bladder disease or peptic ulcer in 1919.

Physical examination showed an obese woman looking about the given age. The abdomen was distended. As there was marked tenderness, a satisfactory pelvic examination could not be done. Rectal exploration did not reveal any abnormality.

The lungs and heart appeared normal. The blood pressure was 130/76. There were no neurological findings, nor was there any indication of a malignancy originating from the breast, the thyroid, or any other accessible organ. X-ray examination showed a moderate distention of the cecum. There were no calculi in the kidneys or the gall bladder. A blood count taken on admission revealed 16,200 white cells, 4.4 million red cells, and 11.5 Gm. hemoglobin. Four days later the white cell count was 12,000. Urine examination showed a trace of albumin, occasional granular casts and white and red blood cells. Electrocardiographic findings indicated moderate myocardial damage and sinus tachycardia.

The patient was operated on Feb. 13, 1947. A large ovarian dermoid was found. It ruptured immediately and discharged caseous fatty fluid, which smelled foul, and also a ball of hair. It was decided merely to drain and marsupialize the cyst, and not to attempt to take it out completely. Examination of the masses removed from the cyst and of a piece of its wall revealed a ball of hairs and gray puttylike material. There was also a toothlike structure. A section taken from the wall contained squamous epithelium with some sebaceous glands, and also some adipose tissue.

The patient made a good recovery and was discharged on March 29, 1947. She was advised to return after some months for final removal of the tumor.

However, she did not come back until June 14, 1951, more than four years after the initial surgery. She had felt well until three weeks prior to this, when a bloody discharge from the abdominal fistula occurred.

Examination revealed the old scar between umbilicus and symphysis from the previous operation, and at the upper end of it a fistula which was surrounded by some papillary proliferations. Blood was oozing out from it. The patient was in a good state of nutrition. The blood pressure was 115/60. Blood studies showed 12,600 white cells, 3.97 million red blood cells, and 11.5 Gm. hemoglobin. The urine contained a trace of albumin.

Diodrast was injected into the fistula. X-ray examination showed a large cyst, apparently not filled completely by the contrast medium and located closer to the anterior wall of the abdomen than to the back.

A biopsy from the border of the fistula was taken. Microscopic examination revealed a squamous-cell carcinoma; there were many mitotic figures.

The patient was operated upon again July 25, 1951. An incision was made around the fistula and the abdomen was opened. There was a large tumor mass, as big as a grapefruit, and another mass, somewhat smaller, adherent to the first one by what seemed to be fibrous tissue. The large mass was firmly adherent to a loop of the ileum; it was necessary to resect about 15 cm. of the intestine, in order to remove the tumor completely.

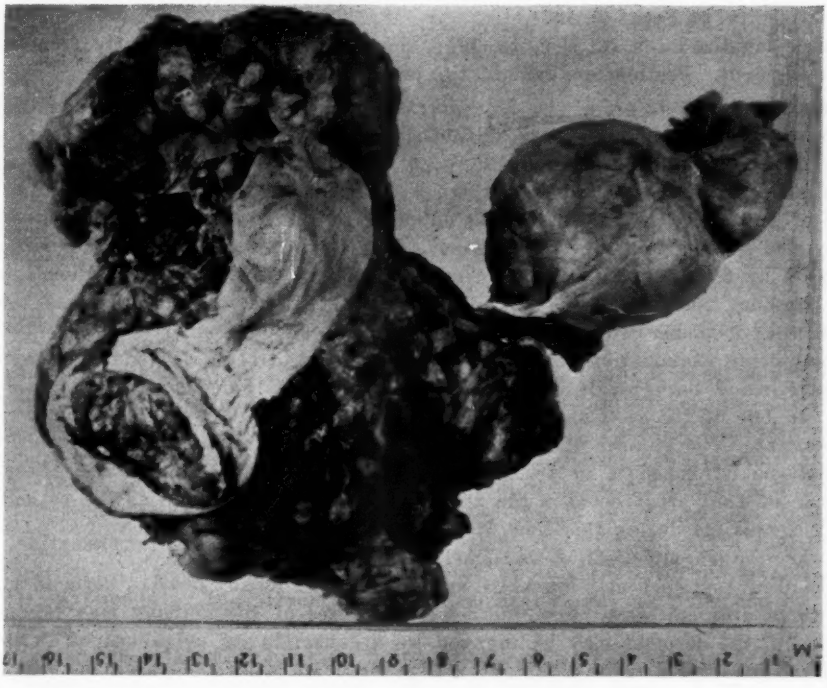

Fig. 1.—Photograph of the specimen removed by operation. Note the skin with the fistula and the two separate tumor nodes.

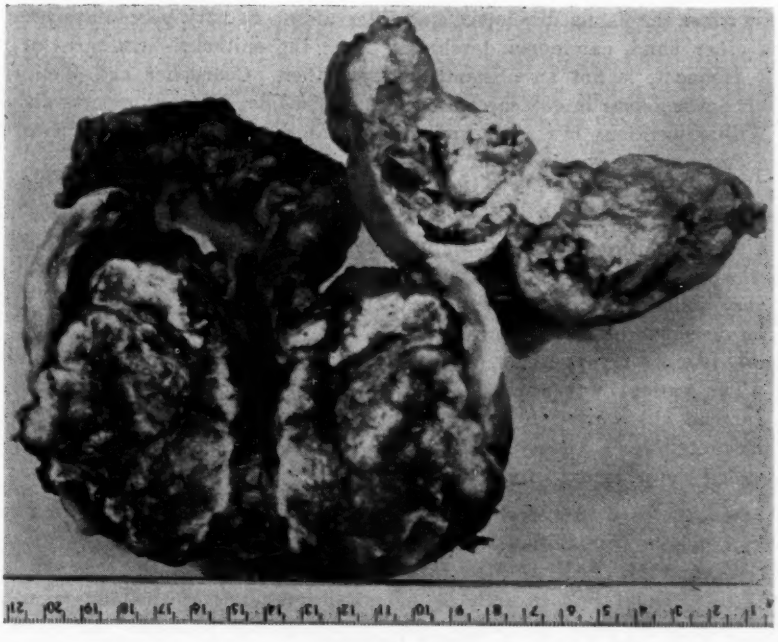

Fig. 2.—Photograph of the nodes opened by dissection. Both nodes are cysts filled with massive proliferations of cancer. On top of the larger node one sees the piece of intestine removed together with it.

The patient made an uneventful recovery after this operation and was discharged from the hospital on Sept. 15, 1951.

Three months later, on Dec. 10, 1951, she died at home, apparently from a cerebrovascular accident. Postmortem examination was not done.

Pathological Description (by Dr. Herman Josephy).—The specimen obtained at the operation consisted of a large mass of tumor, connected with a smaller one by some fibrous strands. The large mass measured 12 by 10 by 6 cm. On one side it was covered by a piece of skin, which in its center exhibited a fistula with ragged and proliferating borders. A piece of bowel, 15 cm. in length, was adherent to it. A surface made by dissecting the node revealed white papillary masses growing into a kind of cyst. The smaller node, which measured 9 by 6 by 4 cm., was partly cystic and partly solid. On dissection it exhibited similar papillary masses like the larger node. Besides that it contained some hair, and a few small bony inclusions which resembled teeth.

Microscopic examination revealed masses of a Grade II to III squamous epithelioma. There were many horn pearls, many atypical cells, and a considerable number of mitotic figures. In one of the sections several small cysts lined by ciliated epithelium were found.

Comment.—The clinical findings and the pathological examination leave no doubt that an epithelioma developed in or from a marsupialized dermoid of the ovary. As there was an interval of four years between the first and second operation and as the patient did not have any complaints during this time, it is justifiable to assume that there was no carcinoma present when the marsupialization was done.

According to Lynch and Maxwell[1] carcinoma found in any ovarian dermoid may originate in three different ways: first, epithelial structures of the dermoid may become malignant; second, the dermoid may be invaded by a cancer in its neighborhood or it may be the seat of metastases from a distant malignancy; and, third, a carcinoma may develop in the ovary proper and invade the dermoid.

Another possibility has to be added for our case, namely, a carcinoma originating from the skin-fistula junction created by the marsupialization.

Carcinoma originating from a fistula, especially from an osteomyelitis, usually appears 20 to 30 years after the fistula developed, and intervals up to fifty years have been reported.[2]

On the other hand, carcinoma developing from the epithelial structures of a dermoid, although not frequent, is not an absolute rarity, either. Counseller and Wellbrock[3] found 1.7 per cent of epitheliomas in 408 cases of ovarian dermoids. Novak[4] reports about the same incidence. Willis[2] mentions five cases and states that most of the malignancies originating from ovarian dermoids are squamous-cell cancers.

As for our case, it is most likely that it belongs in this group of epitheliomas which develop from the "skin" portion of a dermoid. Not only the time interval between the surgical creation of a fistula and appearance of malignancy, but also the fact that the bulk of the tumor was in the abdomen and not around the fistular opening, favor this classification. It seems to be very unlikely that the marsupialization and emptying of the dermoid had anything to do with the development of the malignancy.

Our case, like so many others, stresses the necessity of making the public "cancer conscious." The patient was advised to return for further surgery soon after the first operation. Instead she waited for four years. At this time the carcinoma, which could have been prevented by a timely total removal of the dermoid, had grown into a large mass and invaded the adjacent intestines.

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PRIMARY CERVICAL CHORIOCARCINOMA

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THE present communication is the report of a patient with cervical pregnancy who developed choriocarcinoma, with the clinical and necropsy observations.

The cervix is rarely the site of placental implantation. Fourteen authentic and fourteen presumptive cases of cervical pregnancy were collected from the literature by Studdiford,[1] who added two of his own to the latter group. Dougal[2] reported a patient with cervical pregnancy treated by radical hysterectomy based on a mistaken diagnosis of cervical malignancy. Two cases of cervical pregnancy by Morton[3] and a single case by Schulthiess[4] have been published recently. A case of probable isthmicocervical nidation and gradual extension of the placenta into the cervical canal was described by Bowles.[5] Duckman's[6] case is doubtful.

Choriocarcinoma is an uncommon lesion, even when the placenta is normally implanted. Primary choriocarcinoma of the cervix is extremely rare. A careful résumé of the world literature up to 1915 by Alfieri[7] yielded only twenty-five cases, most of which had undoubtedly begun in the fundus of the uterus and therefore should not be classified as primary cervical choriocarcinoma. In fact, only three cases, his own, and those of Toth[8] and Veit are acceptable. Those of Rosner,[9] Vitrac,[10] Aczel,[11] and Pollosson[12] definitely represent metastatic cervical lesions. The case of Guerard,[13] often described as an authentic case, began as a uterine mole and must therefore be regarded as metastatic. Since 1915, Momigliano[14] reported nine instances and added one of his own. Two of these cases are doubtful. In Meyer's case, prior to the development of the cervical tumor, an intrauterine mole was discovered by curettage. Schimmel interpreted his own case as one of metastasis from the uterus. Another case frequently quoted as cervical choriocarcinoma was published by Bourne.[15] In this case, too, a mole had previously been found within the uterine cavity. Rubin's[16] case is the only one found in the American literature. Thus, there are recorded twelve authentic cases of primary cervical choriocarcinoma in the world literature.

Case Report.—A 38-year-old Puerto Rican woman, para iv, gravida vii, was first admitted to City Hospital on July 18, 1949, with the complaints of amenorrhea since March 18, 1949, low abdominal pain and vaginal bleeding of two weeks' duration. Vaginal bleeding and pain continued after hospitalization. Eleven days later she exhibited delirium, agitation, and excitement, attributed by a neuropsychiatric consultant to a "toxic exhaustive delirious state." On the twelfth day after admission, a fetus measuring 25 cm. was expelled. The placenta was retained, even after intravenous Pitocin. Two weeks later, after a large transfusion of whole blood, curettage was performed. Many large pieces of tissue were removed, which on histological examination proved to be normal placenta. During the procedure, the patient bled profusely and went into shock, which responded to the administration of plasma and blood. Vaginal spotting continued until the eleventh postoperative day, when she was discharged as improved.

She re-entered the hospital eleven months later, on July 14, 1950. Menses had occurred regularly in October, November, and December, 1949, at 28 day intervals, were of five days' duration and of normal amount. In January, 1950, she had two episodes of bleeding of five days' duration each, one week apart. Her last menstrual period had

occurred on Feb. 17, 1950. Following an amenorrhea of five months, on July 7, unassociated with trauma, she noticed small amounts of bright red vaginal bleeding, accompanied by dull, aching, nonradiating left lower quadrant pain.

The temperature was 103.8° F. Examination revealed an obese abdomen with tenderness in the left lower quadrant. There was a moderate-sized cystorectocele. The cervix was posterior, hypertrophied, and patulous, admitting a finger tip. The uterus was thought to be anterior, mobile, soft, and enlarged to the size of a ten weeks' pregnancy. A clinical diagnosis of missed abortion was made. After one week of penicillin therapy, curettage was performed. A moderate amount of placenta-like tissue was removed, which on pathological examination showed trophoblastic tissue without chorionic villi. Massive hemorrhage occurred during the operation, following which the patient went into shock which responded to transfusion. Moderate vaginal bleeding and fever persisted. She was discharged improved on the thirteenth postoperative day.

She was admitted six weeks later, on September 7, for the third time. Continuous staining and diffuse lower abdominal pain had persisted since her discharge from the hospital. A sound could now be passed into the uterus for a distance of four inches. A provisional diagnosis of retained secundines was made and a curettage performed two days later. There was a profuse hemorrhage immediately after the removal of a few fragments of tissue. She developed moderately profound shock from which she recovered after plasma and whole blood transfusion. It was thought that a uterine perforation might have occurred. Microscopic examination of the tissue again showed trophoblastic tissue with absence of chorionic villi.

A stormy postoperative convalescence followed, the temperature varying from 100° to 102° F. The abdomen was distended, with direct and rebound tenderness present. The urinary output was markedly diminished. Her condition improved following abdominal decompression and penicillin and aureomycin therapy. On September 26, there was profuse foul-smelling bloody vaginal discharge. On examination, a posterior colpotomy-like wound was found, through which brownish purulent material exuded. This sinus may have resulted from perforation at curettage. She remained afebrile from September 30 to October 24. Her general condition progressed favorably following numerous transfusions, but the troublesome discharge persisted. Vaginal examination on October 24 revealed the presence of necrotic placenta-like tissue protruding through the dilated cervix. The examination precipitated profuse hemorrhage, necessitating packing and repeated massive transfusions.

A total abdominal hysterectomy and bilateral salpingo-oophorectomy were performed on November 8 under cyclopropane anesthesia. Aside from a brief postoperative bronchopneumonia, her condition continued to improve, so she was in excellent health one week after operation.

Pathology Report.—(37903) *Gross appearance:* The uterus has been removed in toto with attached tubes and ovaries. It measures 15 cm. in length, 9 cm. transversely and 5 cm. in greatest thickness. The major portion consists of a greatly enlarged cervix resembling an angiomatous mass, soft, boggy, and bluish in color. The cervix is lacerated and boggy. The body, which measures 6 by 8 by 4 cm., rests on the cervical mass and presents little of note externally. On opening the uterus (Fig. 1), the cervical canal is filled with soft hemorrhagic tissue resembling placenta; the central portion is necrotic and foul. It is tightly adherent to the thin cervical wall. The site of the "colpotomy wound" found previously during a vaginal examination is not discernible. The junction between cervical canal and uterine cavity cannot be identified. The uterine cavity is small and the endometrium pale tan in color. The tubes and ovaries appear normal.

Microscopy: The entire endocervix, from internal to external os, is replaced by trophoblastic tissue (Fig. 2) with frequent giant cells and bizarre nuclei. Many cells are multinucleated. There is marked cellular, nuclear, and nucleolar anisocytosis and hyperchromatism. Mitoses are moderately abundant and almost invariably bizarre in type. Penetration into the veins by abnormal trophoblastic tissue is a prominent feature. The surface has extensive

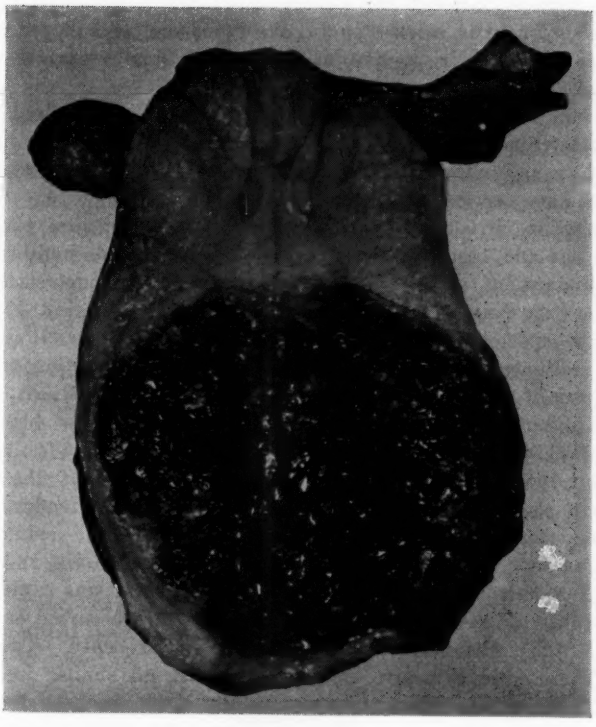

Fig. 1.—The gross appearance of the operative specimen. The canal is enlarged and filled with the hemorrhagic tumor. The body of the uterus is normal.

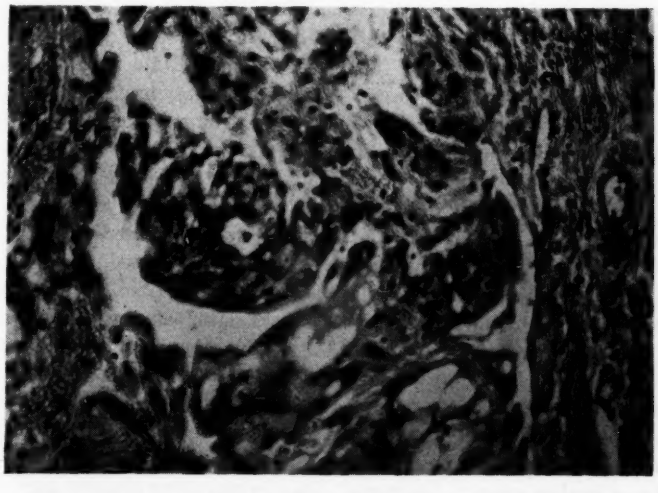

Fig. 2.—Section of the cervical wall showing the trophoblasts invading into the veins and the absence of villi.

necrosis and hemorrhage. The tumor reaches close to the squamocolumnar junction but the junction is preserved and the glands contain the deeply stained mucus seen in pregnancy. The fibrous stroma here is invaded for a very short depth, although penetration into the veins is very marked. There is intense engorgement, edema, and a heavy mixed-cell inflammatory reaction. In the greater portion of the cervix, only a narrow fibrous wall is not invaded by tumor cells.

The endometrium is thin, has a few highly secretory glands and a diffuse decidual reaction. The myometrium is normal. A large corpus luteum with minute focal necroses is present in the right ovary. Otherwise the tubes and ovaries show nothing of note.

Diagnosis.—Primary cervical choriocarcinoma.

Following operation, Friedman tests were performed. At first they were positive in high dilutions, but on one occasion the test was negative with undiluted urine. Several roentgenological examinations of the chest failed to reveal any metastatic lesion. She was referred to the Home Care Service on the forty-second postoperative day.

She remained symptom free for three and one-half weeks, until Jan. 14, 1951, three days before being readmitted for the fourth time because of vomiting and abdominal pain. There was some intermittent substernal pain. Cough, hemoptysis, diarrhea, melena, dysuria, and hematuria were absent.

Examination disclosed moderate epigastric and right lower quadrant tenderness. There was a profuse, foul, yellow vaginal discharge. The left side of the vaginal vault felt irregular and gave a sensation of fullness. Both fornices were tender. Temperature and blood pressure were normal. X-rays of the lungs showed small nodular opacities in the right costophrenic angle. Ten days later these had grown in size and new nodules were seen in both lungs. A Friedman test was positive. The course was rapidly progressive with evidence of bone, brain, and subcutaneous involvement. Death occurred on Feb. 9, 1951.

Autopsy (No. 8726) was performed eleven hours after death. The pertinent findings are summarized. There were extensive metastatic lesions, all similar in appearance, hemorrhagic and friable. Three masses were present in the brain, in both frontal lobes and the superior right parieto-occipital cortex. Five small nodules were present in the right lobe of the thyroid. Both lungs had many small and large masses in the parenchyma and subpleura. One mass was found in the right lobe of the liver. The spleen had a solitary metastasis. The right kidney had many nodules. A large one had penetrated through the capsule and caused a massive retroperitoneal hemorrhage which had displaced the cecum and ascending colon. A solitary tumor was present in the left kidney. The midjejunum had a pedunculated mucosal mass. The vaginal vault was healed but there was a tumor mass in the left parametrium. There were metastases in the ribs.

Anatomical Diagnoses.—Metastatic choriocarcinoma of the parametrial tissues, liver, kidneys, lungs, thyroid, subcutaneous tissue, spleen, jejunum, brain, ribs; massive retroperitoneal hemorrhage from metastasis; previous total hysterectomy and bilateral salpingo-oophorectomy for primary choriocarcinoma of the cervix.

Comment.—It is probable that the pregnancy which terminated with a macerated fetus was a cervical pregnancy, although this cannot be proved. After five menstrual periods had occurred, followed by five months of amenorrhea, vaginal bleeding and dull left lower quadrant pain were noted. Thus the first clinical, but unrecognized, signs of choriocarcinoma became evident nearly one year later. A curettage at this time showed trophoblast tissue without chorionic villi. Another curettage six weeks later also showed similar microscopic findings. Total hysterectomy was performed two months later, for persistent pain and bloody vaginal discharge. At operation, choriocarcinoma was diagnosed and subsequently confirmed by histological examination. She died three months after hysterectomy, eighteen months after the expulsion of a macerated fetus.

Two features presented by this case are worth repetition; their proper evaluation would have led to an earlier correct diagnosis. One outstanding clinical sign was the tendency to severe bleeding, even on the gentlest manipulation, which has been noted and stressed by other observers to be characteristic of cervical pregnancy. On her first admission, she was given 1,500 ml. of blood and 500 ml. of plasma; on the second admission, 1,000 ml. of blood

and 1,000 ml. of plasma; and, on the third admission, 3,250 ml. of blood and 3,000 ml. of plasma, making a total of 5,750 ml. of blood and 2,500 ml. of plasma. The second feature was the microscopic appearance of the curettings. The histological diagnosis of choriocarcinoma from curettings is admittedly difficult. However, the findings of trophoblastic tissue without chorionic villi should have been presumptive evidence of choriocarcinoma. Its duplication a few weeks later, again associated with the clinical feature of massive hemorrhage, probably should have led to the correct diagnosis.

There can be no doubt from the gross and microscopic examination that this is a case of primary choriocarcinoma of the cervix. The origin of this tumor can be discussed only in speculative terms; i.e., whether it originated from the cervical pregnancy which terminated in a macerated fetus, or whether the carcinoma sprang from a subsequent new pregnancy. In favor of the first presumption are (1) an original diagnosis of cervical pregnancy, which is the site of a subsequent choriocarcinoma, (2) the placenta which could not be completely removed might serve as a nidus for malignant transformation, (3) choriocarcinoma may follow abortion with an apparently normal villous pattern. In favor of the second presumption are (1) the apparently normal periods followed by amenorrhea, and (2) the lack of conclusive proof that the pre-existing pregnancy was in the cervix. Against these arguments, however, is the well-known latency in the development of choriocarcinoma and the fact that the amenorrhea may well have been due to the tumor itself. Weighing all these factors, it seems most probable that this patient had a cervical pregnancy with the development of a choriocarcinoma at the site of the adherent placenta.

Summary and Conclusions

1. Cervical choriocarcinoma is an exceedingly rare lesion, only 12 authentic cases being recorded in medical literature.

2. An authentic case of cervical choriocarcinoma is presented with clinical and necropsy findings.

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Department of Reviews and Abstracts

Selected Abstracts

Anesthesia, Analgesia

Neme, B., Onofre Aranjo, J., and Horo, B.: Spinal Anesthesia at the Obstetrical Clinic of the University of São Paulo (Brazil) Medical School, An. brasil. de ginec. 32: 223, Nov., 1951.

The authors observe that the obstetrical anesthesia in 50 per cent of the 487 cases studied was of the spinal type in the aforementioned Brazilian obstetric clinic. The indications for spinal anesthesia were forceps in 36 per cent; cesarean section in 70 per cent; ectopic pregnancy in 77.8 per cent, and fetal destructive operations in 7 per cent. They correlate, by comparative study, spinal anesthesia to other types, and the relationship of blood pressure, blood transfusion, and neonatal asphyxia to the type of anesthesia. They conclude that spinal anesthesia possesses distinct advantages. There were no maternal deaths. The ideal level of spinal anesthesia for obstetric purposes was eleventh or twelfth thoracic for vaginal routes and the eighth to the sixth thoracic for abdominal obstetric surgery. They note a parallelism between the height of anesthesia obtained and the degree of hypotension. They conclude by stressing the critical importance of adequate drug dosage if one is to avoid minor disturbances in blood pressure levels. They noticed 6.9 per cent and 11.8 per cent incidence of neonatal asphyxia in spinal and inhalation anesthetics given to mothers. Numerous tables are given with comparative values of 247 cases wherein spinal anesthesia, 161 cases wherein inhalation anesthesia, 58 cases wherein local anesthesia, and 16 cases where mixed types of obstetric anesthesia were employed.

CLAIR E. FOLSOME.

Cancer, Malignancies

Zuckermann, Conrado: The Stages of Growth of Cancer of the Uterine Cervix, Rev. mex. de cir., ginec. y cáncer, No. 8, p. 235, Aug., 1951.

The author proposes a classification of cervical carcinoma based on the anatomical and clinical evolutionary stages of its development. This classification applies only to epithelial cancer, and cannot be used for the rare cases of cervical cancer of other tissue type (connective, muscular, etc.) because these propagate in a different manner.

Growth and invasion of epithelial cancer in the cervix, as elsewhere, occurs primarily by contiguity and lymphatic extension, and secondarily by the hematogenous route. Connective tissue and muscular cancers also generally extend by contiguity and immediately through blood channels.

The evolutionary stages of cervical carcinoma, clinical and anatomical, macroscopic and microscopic, are indicated by the preoperative findings, modified, rectified, or confirmed by the operative findings and histopathological examination of tissues removed. Frequently the evolutionary stage is more advanced than the clinical findings would indicate.

The author's proposed classification is as follows:

Stage I.—Carcinoma localized to cervix:

A. In situ, preinvasive, intraepithelial, involving the exocervix or the endocervix
B. Of the exocervix, already invasive
C. Of the endocervix, already invasive

Stage II.—Cervical and juxtacervical carcinoma:

A. Of the cervix and vaginal cul-de-sac
B. Of the cervix and juxtacervical parametrium
C. Of the cervix (especially the endocervix) with extension to the endometrium or myometrium

Stage III.—Cervical carcinoma with extension to lymph glands and other pelvic areas:

A. Carcinoma of the cervix and one or more pelvic lymph glands
B. Carcinoma of the cervix with extension to middle third of vagina
C. Carcinoma of the cervix with involvement of one or both parametria to almost their full extent

Stage IV.—Pelvic cancer of uterine origin, with or without distant metastases:

A. Cervical carcinoma with parametrial involvement extending to the pelvic wall, with fixation of uterus and lymphatic propagation;
B. Cervical carcinoma with extension to bladder or rectum; vaginal involvement down to the lower third; pelvic lymphatic propagation
C. Cervical carcinoma extending to other pelvic areas, with propagation to bones, or with extrapelvic ganglionic or visceral metastases

MAGIN SAGARRA.

Deaton, W. Ralph, Jr., and Bradshaw, H. H.: Simple or Radical Mastectomy? South M. J. 44: 1042, 1951.

Treatment of carcinoma of the breast is not a settled issue. Preoperative x-ray irradiation followed by simple mastectomy has recently been advocated in preference to the radical operation of Halsted.

To appraise the result of simple mastectomy, all cases of breast carcinoma at the North Carolina Baptist Hospital seen between 1942 and 1945 have been analyzed. A total of 95 cases was seen, all of which had histologically proved carcinoma of the breast. Fifty-four of these patients were treated by radical mastectomy, with postoperative x-ray irradiation and 24 are still alive after five years, a survival rate of 44.4 per cent. The five-year survival rate for the patients treated by simple mastectomy with preoperative radiation is 54.7 per cent.

The treatment of mammary carcinoma by simple mastectomy, in preference to the radical operation, is based on the theory that complete extirpation of the lesion is never assured except in Stage I lesions and in such lesions by definition a simple mastectomy will suffice. In other words, the radical operation does not remove all of the cancer-bearing tissue in sites remote from the primary lesion and these must be eliminated by irradiation.

WILLIAM BICKERS.

Extrauterine Pregnancy

Zukermann, C.: Ectopic Pregnancy, Rev. mex. de cir., ginec. y cáncer, No. 7, p. 199, July, 1951.

The author reviews the various possible locations of ectopic pregnancy, listing as frequent the tubal (ampullar and isthmic) and tubovarian varieties, as rare the interstitial, infundibular, tuboabdominal and secondarily abdominal gestations, and as very rare the cervical, uterine diverticular, ovarian, intraligamentous, and primary abdominal pregnancies.

The majority of cases are tubal pregnancies: most are in the ampulla, next the isthmic portion of the tube, and last the infundibular or fimbriated end of the tube.

The criteria that make a diagnosis of ovarian pregnancy acceptable are: (1) healthy Fallopian tubes; (2) embryonic sac in the location of the ovary; (3) ovarian tissue as part of the wall of the sac; and (4) uterovarian ligament between sac and uterus.

Concerning the causes of ectopic gestation the author notes that any obstruction in the path of the fertilized ovum may lead to ectopic nidation. He mentions alterations in the ciliated epithelium of the tubes, impaired motility of the tubes, stenosis, kinks, diverticula, etc. Endometriosis may favor nidation in ectopic endometrium. Previous infections, abortions, curettage, the use of pessaries, etc. are mentioned as possible etiological factors.

The author calls attention to the fact that he has frequently observed the coexistence of ectopic gestation with other lesions, such as small cysts of the ovaries, cysts of the tubes, uterine malpositions, myomas, adhesions, etc.

After discussing the symptoms and signs of ectopic gestation, diagnostic procedures, differential diagnosis, causes of error, etc., he states that the diagnosis is often a difficult one. This is evidenced by the fact that those who think of it too much make the diagnosis more often than ectopic pregnancy is really present and, thus, risk doing operations that are unnecessary or not urgent, while those who do not think of it enough often miss the diagnosis and risk not operating in cases which require surgery, often urgently.

In summary, the author states that:

1. The majority of ectopic pregnancies are tubal.
2. Tubal rupture is more frequent than tubal abortion.
3. A correct preoperative diagnosis is made in approximately 70 per cent of cases.
4. The most difficult and frequent differential diagnoses are uterine abortion and adnexal infection.
5. Curettage is performed with relative frequency before the diagnosis of ectopic gestation is made, or in about 10 per cent of cases.
6. Endometriosis has been demonstrated in about 5 per cent of ectopic gestations.
7. Usually the diagnosis is evident at operation, but histopathological examination of tissue removed is necessary, especially if no embryo is identified.
8. Clinically, ectopic gestation is usually seen between the second and fourth months of gravidity.
9. Treatment is almost always surgical. If the operation is performed at the moment of rupture, the most urgent thing is hemostasis.
10. Careful and sufficient transfusions are necessary.

MAGIN SAGARRA.

Gynecology

Sutherland, Arthur M., and Garrey, Matthew M.: Female Genital Tuberculosis: a Twenty-Year Clinical Survey, Glasgow M. J. 32: 231, 1951.

From the Royal Samaritan Hospital for Women at Glasgow comes a review of twenty years' clinical experience with female genital tuberculosis. During the period under consideration 65,943 patients were admitted to the hospital and genital tuberculosis was discovered in 369 of them. This gave an incidence of 0.56 per cent tuberculous involvement of pelvic organs, distributed as follows: endometrium, 48 per cent; Fallopian tube, 37 per cent; ovary, 0.27 per cent; myometrium, 0.27 per cent; cervix, 0.36 per cent; vulva, 0.54 per cent; multiple lesions, 11.92 per cent.

The majority of cases occurred in the lower age group. There were only eight postmenopausal cases, seven of these cases involving the endometrium. A previous history of tuberculous infection, usually pulmonary, was elicited in only seven cases. The most common symptom of which these patients complained was infertility. Pain of various types was the complaint of secondary importance. Normal cyclic menstruation was the rule in most cases.

Genital tuberculosis is on the decline. A comparison of the first and second ten-year periods reveals that gross genital tuberculosis was frequent in the first decade of study and rare in the second. Unsuspected endometrial tuberculosis, usually discovered accidentally in the course of investigation for infertility, was considerably more frequent in the second period of study.

The article is a statistical one and does not describe the mode of treatment at the Hospital from which this report emanates. WILLIAM BICKERS.

Schockaert, J. A.: Tuberculosis of the Endometrium. A Clinical Study of 147 Cases, Minerva ginec. 3: 507, Sept., 1951. Supplement.

The author, director of the Obstetrics and Gynecology Clinic of the University of Louvain, reviews a series of 147 cases of proved tuberculosis of the endometrium. Among these 147 patients, 102 exhibited no palpable clinical pelvic evidence while 45 showed some demonstrable uterine or adnexal pathology to clinical examination.

The author reviews several histopathological criteria, finally noting three principal pathological categories, (1) the miliary micronodular, (2) the ulcerocaseating lesions, and (3) the pseudoneoplastic or epithelioid type.

The age incidence of the 102 patients having no palpable lesions was 15 to 20 years, 4 cases; 21 to 25 years, 14 cases; 26 to 30 years, 26 cases; 31 to 35 years, 36 cases; 36 to 40 years, 16 cases; and 5 cases in the age range of 41 to 55 years.

The dominant syndrome that brought these 102 cases to the attention of the author was sterility in 75 cases (73.5 per cent), menometrorrhagia in 14 cases (14.7 per cent), some type of gynecological pain in 6 cases (5.8 per cent); amenorrhea in 3 cases (2.9 per cent), postabortal hemorrhage and habitual abortion in 2 cases (1.96 per cent). Among the 75 sterility cases, 69 patients had never been pregnant and there were 6 cases of secondary sterility. In the last 50 cases of primary sterility the author was able to demonstrate tuberculosis in 8 patients (16 per cent). There was nonpatency of the tube in 63.3 per cent of this group.

Among the one series of 102 patients exhibiting no palpable pathology, 23 patients (22.5 per cent) had a demonstrable pleuritis and 21 of them also exhibited the initial complaint of sterility. Among those 21 patients were 9 with roentgenographic evidence of healed pulmonary tuberculosis and 12 were demonstrated to have active lesions elsewhere in the body. Three patients had an associated complication of tubercular pelvic abscess or pelvic peritonitis.

The author concludes there should be greater attention directed toward earlier diagnostic measures among which he places endometrial biopsy as of prime importance.

CLAIR E. FOLSOME.

Gysmano, Gaetano: Angioma of the Fallopian Tube, Minerva ginec. 3: 616, Nov., 1951.

The author, from the Institute of Anatomy and Pathology of the University of Genoa, describes a rare case of angioma of the Fallopian Tube. He notes twelve additional cases from the literature. In the case reported the tumor was found incidental to autopsy of a 77-year-old woman who had died from cerebrospinal meningitis. It was the size of a large cherry and localized on the posterior surface of the outer third of the left tube. Three figures illustrate the case report. CLAIR E. FOLSOME.

Labor, Management, Complications

Poulain, P.: Rapid Primiparous Labors (Thiamine Used in Conjunction With Antispasmodics), Bull. Féd. Soc. de gynéc. et obst. de lang. Franç. 3: 630, 1951.

The author, using a method suggested by Shub of Leningrad, studied the effect of giving thiamine along with antispasmodics in a series of primiparous patients. He observed that the degree of analgesia obtained was encouraging in 10 per cent of the cases but

that the length of labor was decreased from 6 to 8 hours in the majority of his cases. His method included giving an initial injection of 50 mg. of thiamine, then an hour later giving a combination injection of 25 mg. of thiamine with Spasmalgin. In 17 cases studied there was complete dilatation obtained in 2 to 3.5 hours in 11 cases, 4 to 7 hours were required in 4 cases, and in 2 cases the complete dilatation had not been reached in 10 to 12 hours. He did observe increased frequency and duration of uterine contractions. A discussant, Beghin, reported he had equally good if not better experience using 100 mg. of thiamine rather than the initial 50 mg. dosage. CLAIR E. FOLSOME.

Brown, Willis E.: The Management of the Borderline Pelvis, South. M. J. 44: 1046, 1951.

The borderline pelvis continues to present a major point of obstetrical indecision. It is the bogeyman of obstetrics. In evaluating the adequacy of any given pelvis, the previous obstetrical history with the length of labor, the weight of the baby, and the type of uterine contractions has significance. Pelvimetry gives limited help and most important is the vaginal examination, preferably done near term when one can evaluate the relationship of the fetal head to the pelvis. The curve of the sacrum, the width of the sacral sciatic notch, the descent of the head, and its relationship to the pelvis can best be estimated by vaginal examination. The anterior-posterior x-ray film and lateral film of the pelvis at this time give the maximum amount of information.

During labor, the patient should be supported by intravenous fluids and a trial labor permitted to continue so long as progress is apparent. When progress ceases, labor must be terminated. The method of termination depends upon the circumstances at hand. If the presenting part is at the inlet, Cesarean section should be done. If the head passes the inlet and comes to rest in the midpelvis, a trial of forceps should be made and, if it fails, abdominal delivery is not contraindicated. The physician must be prepared to terminate labor by either the vaginal or abdominal route and he must be willing to lay down the forceps and pick up the scalpel. WILLIAM BICKERS.

Ravina, J., Jamain, B., and Bonhomme, J.: Spontaneous Rupture of the Symphysis Pubis in the Course of Normal Delivery of a Large Infant, Bull. Assoc. de gynéc. et obst. de lang. franç. 1: 500, 1949.

The authors cite a case report of a patient, para v, whose symphysis pubis was ruptured spontaneously during delivery of an infant weighing 5,250 grams after an half-hour of total labor. The day following delivery the patient exhibited pain over the symphysis. This was associated with edema and tenderness over this area and at least 2 fingerbreadths' separation. X-rays confirmed the diagnosis. Treatment consisted of local infiltration of Novocain, calcium glucuronate, vitamin D, and immobilization of the pelvis for 70 days.

Five photographs of the roentgenograms are included. CLAIR E. FOLSOME.

Miscellaneous

Albers, H.: The Relationship Between Ascorbic Acid and Blood Iron Metabolism, Zentralbl. f. Gynäk. 73: 995, 1951.

The relationship between iron metabolism and vitamin C has been studied at the author's clinic since 1942. It has been well established that when iron preparations are given concomitantly with vitamin C there appears to be a greater absorption of iron into the blood and serum than when iron is given alone. The authors raised the question as to the exact action of the vitamin C in producing this result. In a review of the literature it has been amply demonstrated that the ferrous form of iron is more easily absorbed and in greater quantities than the ferric form. It has been thought by others that the action of the vitamin C in the intestine is either to prevent the oxidation of the ferrous iron to the ferric iron, or in some manner to allow the ferric iron to be reduced to the ferrous form. In a series of experiments on healthy pregnant and nonpregnant women, the authors have found that with

the ingestion of vitamin C there is a definite increase in both the blood and serum iron. They also found that this increase occurred even in fasting women. Furthermore they noted that in those women who were not fasting there was an initial rise in blood iron which was followed later by a secondary rise. They feel, therefore, that the action of vitamin C is partially upon stored depots of iron in the body. They reached the conclusion, therefore, that beside the extrinsic intestine factor that asorbic acid acts in the following way in the treatment of iron deficiency and anemias: First, by action upon the iron preparation itself in maintaining the bivalent form in the intestine; second, in some manner it is able to cause the reduction of the ferric to the ferrous form; third, beside this reducing effect on the iron, the ascorbic acid has an effect on the organism itself which results in a marked increase in serum iron, independently of iron absorption, and is related to the liberation of storage depots of iron in the body.

L. B. WINKELSTEIN.

Newborn

Tinne, J. E., and Henderson, J. L.: Primary Streptomycin-Resistant Tuberculosis in a Newborn Child, The Lancet 2: 901, Dec. 30, 1950.

During treatment of tuberculosis, streptomycin resistance develops slowly. It is almost never encountered before the treatment is started, is seldom demonstrable in the first month, is present in 13 per cent of cases during the second month, 29 per cent of cases after 90 days, and in 43 per cent after 120 days. The authors report the clinical course of an 11-week-old infant, hospitalized with miliary tuberculosis, who died after 11 days of intensive streptomycin therapy. Studies of the organism showed a very high degree of streptomycin resistance at the onset and at the end of therapy. The authors believe that primary streptomycin resistance is due to a previous passage of the organism through a host treated with streptomycin. Therefore, cases such as that here reported may become less rare.

A simple vertical diffusion streptomycin-sensitivity test is described. This demonstrates higher degrees of streptomycin resistance than does the standard Dubos test, and also indicates the number of resistant variants present.

IRVING L. FRANK.

Blackman, J. H.: Rare Congenital Malformations in Two Newborn Infants, Bull. Féd. Soc. de gynéc. et obst. de lang. franç. 1: 560, 1949.

The author describes in detail two unusual gross congenital anomalies. The first infant exhibited a large area of venous telangiectasis along the sagittal suture of the cranium. The second infant showed a segmental agenesia of the left femur. The left femur was approximately only one-half as long as that on the right. The lesion of the former infant was excised surgically.

CLAIR E. FOLSOME.

Howarth, B. E.: Epidemic of Aniline Methaemoglobinaemia in Newborn Babies, The Lancet 1: 934, Apr. 28, 1951.

An outbreak of methemoglobinemia, involving a premature baby unit and some of the nurseries of a maternity hospital, is described. Twenty-three babies were affected, and developed a slate-blue color and restlessness. There was no dyspnea or feeding disturbance. The condition was traced to the use of new unwashed diapers on which a trade name had been printed with an aniline dye. Absorption had occurred through the skin and the effects appeared earlier in babies with excoriated buttocks.

One or 2 c.c. of 1 per cent methylene blue, intravenously, produced an immediate and dramatic response, and the baby so treated looked well within an hour. Babies given ascorbic acid by mouth fared no better that a group of untreated babies. Many babies developed reticulocytosis and mild anemia, especially in the premature unit. Four prematures required transfusions, and one infant died two months later, with enteritis, thrombophlebitis of the portal vein, and splenomegaly.

Nine similar outbreaks, affecting a total of eighty-two infants, have been previously reported.

IRVING L. FRANK.

Pregnancy, Complications

Alesbury, Robert Johnson: Bacteriology of the Urine in Late Pregnancy and at Delivery in Relation to Puerperal Urinary Tract Infection, Western J. Surg., 60: 54, 1952.

The female urinary tract is peculiarly susceptible to infection. The short urethra, the relatively incompetent sphincter, the proximity to reproductive and the lower gastrointestinal tracts, the atony associated with pregnancy, and the pressure of pelvic tumors or the pregnant uterus all play important roles.

An effort was made in this study to correlate frequency of positive urine cultures in the last four to six weeks of pregnancy with the incidence of positive urine cultures at the time of delivery and with the incidence of postpartum urinary tract infections. Urine was taken for culture during the last four to six weeks of pregnancy. The types of organisms found varied considerably. The streptococci were the organisms most frequently encountered. The next most common were the organisms of the *Escherichia coli* group, and last the *Staphylococcus aureus.* The length of labor, the method of delivery, or catheterization during labor played little part in subsequent development of infection. A positive culture from urine collected at the time of delivery aids in prognosticating puerperal urinary tract infection. Cultures taken in the last four to six weeks give no indication of impending puerperal urinary tract infection. WILLIAM BICKERS.

Da Costa Barros, Albertino: Placenta Previa, Rev. port. obst. ginec. e cir. 4: 357, Nov.-Dec., 1951.

The author, in his doctoral thesis, continues the second half of his extensive review on the subject of placenta previa with a report upon the experience with this obstetrical problem at the Obstetric Clinic of the Coimbra Medical School. In a twenty-year period, 1931 to 1951, there were 242 cases of placenta previa. This complication of pregnancy was present in 25 per cent of their deliveries. The first half of the literature review of his doctoral thesis may be found in Vol. 4, No. 5, page 324, of the same journal.

The author observes that while the incidence of placenta previa is in the region of 1 to each 1,000 deliveries in the general obstetrical statistics the incidence in maternity hospitals ranges 3 to 10 per cent because of the concentration of more problem cases. In Coimbra Clinic, however, the incidence is 25 per cent because the clinic tends to serve only the more complicated obstetrical cases from the whole central area of Portugal.

The author employs F. J. Browne's classification of placenta previa and notes the following distribution: Type I, 29 per cent; Type II, 29.5 per cent; Type III, 31 per cent, and Type IV, 10 per cent—from the 236 cases classified. In six additional cases there were inadequate data. Barros considers Browne's classification more adequate as an international method for describing the varieties of placenta previa. He found repeat placenta previa in the same patient rare, 1.2 per cent in his series. The author found that 31 patients, 13 per cent, entered the clinic before labor, and 211 cases, 87 per cent, arrived in some stage of labor.

Forty cases of previa were treated by artificial rupture of the membranes; 79 per cent of these were Type I, 13 per cent were Type II, and 8 per cent were Type III. There were no maternal deaths in this subgroup although there was 7.5 per cent morbidity. There was a 22.6 per cent fetal mortality, 20 per cent of which was immediate.

Sixty-one women were treated by the Puzos-Pinard method, conversion to a breech and bringing down one or both feet as a tamponade, with a maternal mortality of 1.6 per cent and a morbidity of 26 per cent. The distribution of the clinical types in this subseries were Type I, 31 per cent, Type II, 42.6 per cent, and Type III, 26 per cent. In this group was an over-all fetal mortality of 49 per cent, of which 44 per cent was immediate. Eighteen per cent of this subseries, however, were infants who weighed less than 1,800 grams.

Forty-three patients were treated by using the Willett forceps method in the following clinical categories: Type I, 5 per cent; Type II, 37.5 per cent; Type III, 55 per cent; and

Type IV, 2.5 per cent. The maternal death rate was 2.3 per cent with a 34.6 per cent maternal morbidity. The total fetal mortality of this subgroup was 84 per cent of which 79 per cent was immediate. Thirty per cent of these infants weighed less than 1,800 grams.

There were 14 cases treated by classical section and 14 additional cases in which the low cervical section was used. The clinical types treated by classical section were Type I, 23 per cent; Type II, 15 per cent; Type III, 38.4 per cent; and Type IV, 23 per cent. Maternal mortality and morbidity from classical section were 14.2 per cent and 33.3 per cent, respectively. The over-all fetal mortality by classical section was 7.1 per cent and all infant deaths were immediate. The distribution of clinical types in 14 cases treated by low cervical sections was: Type I, 14.2 per cent; Type III, 21.4 per cent; and Type IV, 64 per cent. Maternal mortality and morbidity were 14.2 per cent and 15.3 per cent, respectively, while the infant total mortality was 28.4 per cent, half of which was immediate and half neonatal.

Braxton Hicks version and extraction was employed in 17 women with a maternal mortality of 29 per cent and morbidity of 33.3 per cent. All infants delivered by Braxton Hicks method were dead on birth or died soon afterward.

In the remaining 32 cases the placenta previa was treated by bags, embryotomy, hysterectomy, or combinations of these with Simpson forceps delivery.

The over-all maternal mortality was 5.9 per cent and the morbidity of the 236 mothers was 22.0 per cent. The over-all fetal mortality was 58.4 per cent of which all but 4.6 per cent was immediate.

The author observed that the mortality rate of 180 mothers whose systolic blood pressure exceeded 100 mm. Hg was 1.6 per cent; 12.2 per cent of the 41 patients having systolic blood pressures between 100 and 70 mm. Hg; and 40 per cent maternal mortality in the 15 mothers whose systolic blood pressure was under 70 mm. Hg.

The author documents each of 236 of the total 242 cases with a concise history. The bibliography is excellent. It is well to recall that in this Clinic 1 of every 4 cases attended exhibited definite placenta previa.

CLAIR E. FOLSOME.

Pregnancy, Physiology

Brzezinski, A., Bromberg, Y. M., and Braun, K.: Riboflavin Excretion During Pregnancy and Early Lactation, J. Lab. & Clin. Med. 39: 84, 1952.

This interesting study on riboflavin excretion is reported from Jerusalem, Israel, where pregnant patients and nonpregnant controls were studied under conditions of dietary restriction and compared with similar groups on an adequate diet.

These workers noted a distinctly lower riboflavin excretion in pregnant over nonpregnant individuals with a decrease in the last trimester. It was clear that clinical manifestations of riboflavin deficiency occurred frequently in pregnant women with low intake, which did not appear in nonpregnant patients on the same diet. The results also indicate that the riboflavin requirement is increased during lactation, but is not as high as that during pregnancy.

S. B. GUSBERG.

Nolan, James J., and Pollak, Otakar J.: The Ectocervix During Gestation, Surg., Gynec. & Obst. **93:** 609, 1951.

Seventy-five patients at various stages of pregnancy were studied with regard to the morphological appearance of the cervix by means of punch biopsy. No instance of intra-epithelial carcinoma or alterations suggesting neoplasm were observed. Two major changes were present in the glands during gestation: one, a papillary intra-acinar hyperplasia characterized by long thin projections of the mucosa, and, two, a multiplicity of nuclear layers, which can appear in an isolated patch of the mucosa. No changes were observed which resembled adenocarcinoma.

Hypertrophy of the ectocervical lining was ascribed to mid-zone changes rather than basal-layer activity. Other changes in the squamous lining were, one, irregularity of basal

nuclei; two, disturbed polarity of basal cells; three, variation in the shape of the cells and nuclei; four, an increased number of nuclei; five, mitotic activity; six, budding of the epithelium; and seven, thickening of the basal-cell layer. L. M. HELLMAN.

Nesbitt, Robert E. L., Jr., and Hellman, Louis M.: The Histopathology and Cytology of the Cervix in Pregnancy, Surg., Gynec. & Obst. **94**: 10, 1951.

This is a study of cervical biopsies and smears from 300 pregnant women. The safety of cervical biopsy during pregnancy is attested by the figures given. The authors noted basal-cell hyperactivity in 6.8 per cent, gland hyperplasia in 28.7 per cent, gland epithelial hyperplasia in 47.4 per cent, adenomatous hyperplasia of the glands in 44.1 per cent, epidermization in 62.7 per cent, basal-cell hyperactivity in epidermization in 10.7 per cent, and intraepithelial carcinoma in 0.66 per cent. Upon study of the smears normal parabasal cells were seen in 92.2 per cent and abnormal parabasal cells in 20.5 per cent of the cases. There was a definite correlation between the occurrence of parabasal cells in the smear and basal-cell hyperactivity of the biopsy. These changes regress within 7 to 12 weeks post partum. Caution should be exercised in the assessment and treatment of cases diagnosed as intraepithelial carcinoma during pregnancy. L. M. HELLMAN.

Braitenberg, H.: Effect of Histamine on the Circulatory System During Pregnant and Nonpregnant States, Wien. klin. Wchnschr. **63**: 943, 1951.

Histamine and histamine-related compounds were studied in pregnant and nonpregnant women. When a woman becomes pregnant, the histamine substance in the blood rises rapidly, and reaches its maximal level at the seventh month. From this time, the level rapidly decreases, so that by the ninth postpartum day it is at the normal nonpregnant level. The rise in early pregnancy is so marked that it is felt that the quantitative determination is as accurate, or more accurate, than the Aschheim-Zondek test for the diagnosis of early pregnancy. Ten normal and ten pregnant women were studied. The authors found that in the nonpregnant states, injection of Imido (Roche) given in 1 c.c. doses subcutaneously resulted in a fall in blood pressure of approximately 7 per cent in the lying position and 10 per cent in the standing position. This drop reached its maximum in 70 to 80 minutes. On the other hand, during pregnancy the effect had already reached its maximal and had completely disappeared after 30 to 40 minutes. Where a low blood pressure already exists, probably due to increased amounts of histamine, the injection of further histamine may produce collapse in a normal woman. This effect is not noted in pregnant women with hypotension. The interpretation of this difference is thought to be due to the changes in histamine and histaminase compounds in the blood. L. B. WINKELSTEIN.

Puerperium

Lorenz, Siefried: The Dangers of Partial Placental Retention After Delivery and Methods of Treatment, Zentralbl. f. Gynäk. **73**: 1337, 1951.

In normal delivery the placenta is usually delivered spontaneously or is removed by the Credé maneuver. There is no danger in leaving the placenta in the uterus for a short time following delivery providing no bleeding is present, but it should be removed manually after a reasonable length of time has passed. It often occurs that with too forceful attempts at removing the placenta portions are left in the uterine cavity (3 times more frequent). Other conditions such as changes in the uterine lining, fibroids, cornual implantation, placenta previa, hydramnios, and partial accreta result in nondetachment of portions of placental tissue. Infections such as syphilis, gonorrhea, endometritis, and changes such as decreased hormone function may have something to do with the retention of all or a portion of the afterbirth. Therefore, in all cases, after the third stage of delivery is completed, the placenta should be thoroughly inspected for absent portions. This is especially true when any of the

above conditions are present, when a history of retained or abnormal delivery of the placenta at a previous delivery is elicited, or when the placenta is unusually large or presents any pathological features.

Retained portions of the placenta may result in atony of the uterus, uterine apoplexy, most severe hemorrhage, infection, and even death.

After diagnosis is made immediately after delivery, if no morbidity is present, the retained portions should be removed immediately, either digitally or by means of a dull curette. No danger is present if this procedure is carried out aseptically and there is reasonable assurance that the uterine cavity has not become infected. The procedure is so safe that curettage should be attempted even if hemorrhage is not thought to be due to retention except when uterine atony is present, when previous uterine scars are present, or when the size of the retained portion is larger than a hand.

When fever or other contraindications for curettage exist, sponge stick or digital removal is indicated. With retained portions the morbidity is 90 per cent and mortality 30 per cent, and therefore the abdominal approach may sometimes have to be considered. However, with the adequate use of the sulfonamides and the antibiotics the dangers of infection are markedly decreased and when these are given prophylactically the only danger is from hemorrhage and less grave surgical procedures may be utilized. L. B. WINKELSTEIN.

Sterility

Freeth, Derek: Hysterosalpingography in Female Infertlity, The Lancet 1: 15, Jan. 5, 1952.

The author gives a historical review of the use of hysterosalpingography in sterility diagnosis and stresses its advantages over gaseous insufflation. He then goes on to discuss the advantages of water-soluble contrast media over Lipiodol and similar oily substances; the principal disadvantages of the latter group are said to be (a) foreign body reaction, (b) flare-up of pelvic inflammation, (c) oil emboli.

This interesting paper then goes on to discuss the advantages in nontoxicity and water solubility of Viskiosol Six (50 per cent diodone with 6 per cent polyvinyl alcohol) and to present 100 patients studied by this technique with an equal number of Lipiodol-studied patients for control. In addition to nontoxicity, it appears that the author was able to obtain a clearer end point for tubal patency with this watery substance, and to overcome tubal spasm shown on gaseous insufflation in some cases.

Of the 100 patients studied with Viskiosol Six it is concluded that pregnancy in five could be directly attributed to the investigation. S. B. GUSBERG.

Lambillon, J., and Drumel, G.: Contribution to the Study of Sterility Among the Indigenous Population of Leopoldville, Bull. Féd. Soc. de gynéc. et obst. de lang, franç, 3: 566, 1951.

The demographic distribution of the indigenous populations of the Belgian Congo is daily becoming increasingly important. In selected areas of the central area of the Congo the local tribes are overpopulated, especially in certain areas of Ruanda-Urundi and parts of Kivu. But in other areas and certain tribes showing better physical and intellectual qualities there is a disquieting, relatively rapid decrease in population, notably among the Mongos peoples. The authors report upon their findings among 978 native women presenting problems of infertility for the single year of 1949 at the gynecological service in Leopoldville.

Among these 978 cases were 665 cases of primary sterility in women married less than 2 years and yet who had not become pregnant; 260 cases of secondary sterility wherein the patients had one or more pregnancies at least 3 years previously and a small group of 53 cases wherein the patients gave histories of habitual abortion.

Gynecological examination revealed in the 978 patients the following distribution of pelvic findings: (1) a cervical factor in 87 cases (9 per cent); (2) normal pelvis in 127 cases (14 per cent); (3) infantile uterus in 60 cases; (4) degenerating fibroids in 42 cases;

(5) acute anteflexion in 8 cases; (6) movable retroversion in 142 cases; (7) adherent retroflexion with adnexitis in 177 cases; (8) adnexitis in 325 cases; and (9) pelvic peritonitis in 10 cases.

The authors did 724 tubal insufflations, 399 upon diagnostic indications and 325 for therapeutic or control measures. Among the 399 diagnostic tubal insufflations done in 263 primary sterility and 136 secondary sterility cases were the following findings: (1) primary sterility group—57 per cent had nonpatent tubes; 21.2 per cent had partially stenosed tubes; while 21.8 per cent exhibited normal tubal patency; in the (2) secondary sterility group it was noted that 46 per cent had nonpatent tubes, 27 per cent had partial tubal stenosis, and 27 per cent evidenced normal tubal patency. In short, some aberration or complete loss of tubal patency was present in approximately 75 per cent of the patients.

There were 123 cases selected for endometrial biopsy to study the endometria. Among the 85 patients in the primary sterility group in this subseries, 42 per cent, 34 cases, exhibited abnormal endometria, while the remaining 51 patients, 58 per cent, had normal secretory endometria. In the subseries of 38 cases of secondary sterility the endometrium was found abnormal in 20 cases, 52 per cent, and normally secretory in 18 cases, 48 per cent.

There were 96 male semen specimens examined, of which 68 per cent were normal, 14 per cent were oligospermic, 11 per cent were astheno-oligospermic, and 7 per cent were azoospermic. Among the 21 testicular biopsies studied were 18 showing normal spermatogenesis and 3 with atypical spermatogenesis. In short, the masculine factor, using the above subseries as a criterion, would seem to be approximately responsible in 15 to 20 per cent of the couples.

In the series of 53 habitual abortion cases were 25 patients with retroversion, 8 with uterine fibroids, 4 with cervical stenosis, and one who exhibited a cervical polyp. In 13 cases no clinically abnormal finding could be demonstrated.

Among the total series, in this short space of study, one year, the authors were able to report 38 women who had become pregnant after variable types of therapy. Twenty-one of these cases were from the primary sterility group and 17 were from the secondary sterility group.

In conclusion, the authors state that among 925 cases of sterility it was possible to demonstrate one or more factors in 97 per cent of the series according to this distribution: (1) vaginal or cervical pathology in 3.8 per cent, (2) infantile uteri in 3.0 per cent; (3) uterine malposition or fibroids in 9 per cent; (4) associated or mixed clinical lesions 5.7 per cent; (5) pre-existing or existing pelvic inflammatory disease disturbing tubal patency in 69.6 per cent; (6) anomalous hormonal disturbance in 6 per cent; and (7) undetermined factors in 3 per cent. The article is well documented with figures and statistical tables.

CLAIR E. FOLSOME.

Mengert, William F.: Sterility, South. M. J. 44: 1050, 1951.

This article presents an intelligent, rational, and comprehensive review of the essential factors worthy of consideration in the management of the infertile couple. First, the anticipatory parents are interviewed singly and as a couple. The general physical status of each is evaluated on the basis of history and a complete physical examination. Symptomatic treatment for infertility is cruel because the physician is dealing with powerful and fundamental human emotions and fears which cannot possibly be allayed without careful and painstaking diagnostic effort.

The male must be capable of producing normal and motile sperm in adequate quantity and further must be able to deposit this sperm in or near the external cervical os. The miscibility of the cervical secretions with the semen must be determined.

The female must have the capacity for the production of ova, capable of fertilization, and functioning Fallopian tubes which may serve as a conduit for sperm and at the same time actively propel the zygote. Correctable defects such as cervical disease should be remedied and many authorities believe that myomectomy is justifiable, even when the position

of the myoma seems noncontributory. Conservative operation for endometriosis may be indicated, but, conversely, there is little to justify suspension of the uterus for uncomplicated retroversion.

Treatment of the subfertile male centers around emotional and physical rest, and most authorities are virtually unanimous that these are the only measures of real benefit when the sperm counts and motility are low or abnormal forms high.

The suction curette biopsy at the onset of menstruation provides the best means for determining the presence or absence of ovulation in any given cycle. The basal body temperature is an aid in fixing the time of ovulation. Where ovulation fails to occur, resection of a wedge of each ovary or low-dose irradiation has been suggested, but neither is recommended by the author.

Patency of the Fallopian tubes is best determined by carbon dioxide insufflation. Hysterosalpingography sometimes gives additional information.

A number of practical questions were put to the author during the discussion, after the presentation of this paper, and his answers are pointed, positive, and poignant.

WILLIAM BICKERS.

Venereal Diseases

Macfarlane, W. V.: Treatment of Syphilis During Pregnancy, The Lancet 1: 1069, June 10, 1950.

The Venereal Diseases Department of Newcastle General Hospital in England treats syphilitic patients who come from a large urban, rural, and seaport area. Gravid women tend to report rather late in pregnancy and to default on treatment schedules. Treatment consisted of a combination of penicillin, arsenic, and bismuth (''P. A. B. unit''). Arsenic (Novarsenobillon or Stabilarsan) was given in a total intravenous dosage of 4.65 Gm. in a nine-week period; bismuth oxychloride intramuscularly in a total dose of 2.6 Gm. in a thirteen-week overlapping period and penicillin in a total intramuscular dosage of 2.4 to 3 million units before, during, or after the other medications.

Of 300 pregnant women so treated, 44 per cent had primary or secondary syphilis, 41 per cent had latent syphilis, 13 per cent had congenital syphilis, and 2 per cent had tertiary lesions. All patients received the full penicillin course and at least one-fourth of the heavy metal therapy. There were five abortions, five stillbirths, five neonatal deaths, and five infant deaths under the first year. These figures are comparable with fetal loss rates in nonsyphilitic patients in this area. It is remarked that the fetal salvage rate does not seem to be worse in those patients whose treatment was started late in pregnancy.

IRVING L. FRANK.

Items

American Board of Obstetrics and Gynecology

The following candidates were certified by the American Board of Obstetrics and Gynecology, June 13, 1952, at The Drake Hotel, Chicago, Ill.

Abelow, Irving	310 East Seventy-fifth St.	New York City 21.
Adair, Robin	1016 North Hunter St.	Birmingham, Mich.
Albers, Millard J.	715 Court St.	Saginaw, Mich.
Aldridge, Charles W., Jr.	110 North Durkee St.	Appleton, Wis.
Algozer, Alfonso L.	1353 Putnam Ave.	Brooklyn, N. Y.
Anderson, Hugh R.	15648 Madison Ave.	Lakewood, Ohio
Andrews, Mason C.	605 Medical Arts Bldg.	Norfolk, Va.
Baker, Thomas H.	130 North La Cienega Blvd.	Los Angeles, Calif.
Barno, Alex	4959 Excelsior Blvd.	Minneapolis, Minn.
Barrick, Robert G.	2051 North Sedgwick St.	Chicago, Ill.
Bayly, Melvin A.	720 North Michigan Ave.	Chicago, Ill.
Bell, Thomas G.	211 West Frederick St.	Staunton, Va.
Bicek, Joseph F.	350 St. Peter St.	St. Paul, Minn.
Blahey, Peter R.	1374 Sherbrooke St., West	Montreal, Quebec
Bland, C. Brinley	Episcopal Hospital	Philadelphia, Pa.
Brady, John B.	900 Seventeenth St., N. W.	Washington, D. C.
Brandes, Robert W.	1101 Main St.	Peoria, Ill.
Brannen, Edmund A.	875 Hemlock St.	Macon, Ga.
Breese, Melvin W.	833 Southwest Eleventh Ave.	Portland, Ore.
Brown, James M.	916 Fourth Ave.	Tuscaloosa, Ala.
Brown, Leonard	24 Salem St.	Hackensack, N. J.
Brown, Maurice L.	269 South Nineteenth St.	Philadelphia, Pa.
Brown, Robert G.	2946 Broadway	Redwood City, Calif.
Brubaker, Elwood R.	311 Penn Ave.	West Reading, Pa.
Brumfield, Fred O.	2809 Napoleon Ave.	New Orleans, La.
Bruns, Paul D.	4200 East Ninth Ave.	Denver, Colo.
Buckley, Arthur F.	105 Arnold St.	New Bedford, Mass.
Byrd, William E.	327 West Bute St.	Norfolk, Va.
Calderwood, George C.	United States Naval Hospital	Quonset Point, R. I.
Calvert, Kenneth G.	904 Greyhound Bldg.	Calgary, Alberta
Cannizzaro, Franklin J.	One Flamingo	Levittown, N. Y.
Capalbo, John L.	847 Eastern Parkway	Brooklyn, N. Y.
Cavanaugh, Thomas E., Jr.	1180 Beacon St.	Brookline, Mass.
Charvet, Leonard W.	2241 Central Ave.	Alameda, Calif.
Cheney, Charles B.	64 Trumbull St.	New Haven, Conn.
Clark, Richard N.	6253 Hollywood Blvd.	Hollywood, Calif.
Clifford, William S.	518 Murrah Bldg.	Columbus, Ga.
Conan, Mark E.	713 East Genesee St.	Syracuse, N. Y.
Connelly, John J.	704 Fourth St.	Niagara Falls, N. Y.
Crissey, Robert R.	101 West John St.	Bay City, Mich.
Crites, John L.	221 Morris St.	Charleston, W. Va.
Dacus, Robert M., Jr.	200 East North St.	Greenville, S. C.
Dana, Ethel S.	1339 North Redwood Ave.	San Jose, Calif.
Daniel, John F.	1204 Medical Arts Bldg.	Oklahoma City, Okla.
Day, Charles W.	1420 Seneca	Seattle, Wash.
de Quevedo, Nestor G.	208 Medical Arts Bldg.	Scranton, Pa.
Dreyer, Carl J.	3821 Utah Place	St. Louis, Mo.
Edmondson, Robert B.	18501 Mack Ave.	Detroit, Mich.
Eubank, William P.	1116 Heyburn Bldg.	Louisville, Ky.

Evans, George L.	30 South Mulberry St.	Mansfield, Ohio
Everhart, Wilson C.	125 State St.	Harrisburg, Pa.
Fino, Julius A.	Four Pennsylvania Ave., West	Warren, Pa.
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Frachtman, Kurt G.	450 West End Ave.	New York City
Fralick, Charles E.	923 South Limestone St.	Springfield, Ohio
Fried, Paul H.	1812 Spruce St.	Philadelphia, Pa.
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Gilmore, Harry L., Jr.	716 East Jefferson St.	Syracuse, N. Y.
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Greenblat, Bernard	23 Schenck Ave.	Great Neck, L. I., N. Y.
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Haines, Hilton D.	118 South Lawrence St.	Rockingham, N. C.
Hankins, Joseph B.	20 West Fifth Ave.	Lexington, N. C.
Hapke, Fred B.	350 East Broad St.	Columbus, Ohio
Hardie, Gilbert S.	2113 Fifth Ave.	San Diego, Calif.
Harsh, Ralph T.	770 Paulsen Medical Bldg.	Spokane, Wash.
Hartnett, Dalton C.	634 North Grand Ave.	St. Louis, Mo.
Hawks, Graham G.	133 East Eightieth St.	New York City
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Hellwig, Edward F.	679 West Market St.	Akron, Ohio
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Jacoby, Ben E.	Nine Buttles Ave.	Columbus, Ohio
Jondahl, Willis H.	324 East Harrison Ave.	Harlingen, Texas
Jones, Brock D., Jr.	1204 Colonial Ave.	Norfolk, Va.
Jones, Edward G.	635 Westlake Ave.	Los Angeles, Calif.
Kant, Emanuel R.	240 High St.	Perth Amboy, N. J.
Kaufman, Sherwin A.	59 East Fifty-fourth St.	New York City
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Lamar, Robert F.	6127 Forest Ave.	Kansas City, Mo.
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Lazar, Morton R.	7401 Third Ave.	Detroit, Mich.
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Lelich, Bronko P.	USAF Hospital, Lackland Air Force Base	San Antonio, Texas
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Smith, Louis S.	244 Primrose Ave.	Mt. Vernon, N. Y.
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Wright, Ralph C.	32 Grove Hill	New Britain, Conn.
Young, Claude C., Jr.	126 Southeast Seventh St.	Evansville, Ind.
Zeit, Paul R.	11406 Euclid Ave.	Cleveland, Ohio

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ROBERT L. FAULKNER, M.D., SECRETARY
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American Board of Obstetrics and Gynecology

The American Board of Obstetrics and Gynecology wishes to announce the election of the following officers at its recent annual meeting, held in Chicago, Ill., June 7-13, 1952:

President—Walter T. Dannreuther, M.D., New York City
Vice President—F. Bayard Carter, M.D., Durham, N. C.
Vice President—Robert A. Kimbrough, Jr., M.D., Philadelphia, Pa.
Secretary-Treasurer—Robert L. Faulkner, M.D., Cleveland, Ohio
Assistant Secretary—Lawrence M. Randall, M.D., Rochester, Minn.
Member Executive Committee—Herbert E. Schmitz, M.D., Chicago, Ill.

Of special interest to candidates for admission to the examinations for certification by the Board will be the following requirement, which was adopted at the meeting: Candidates currently applying for admission to the examinations for certification are required to submit a list of all patients admitted to the hospitals where they practice, for the year preceding their application or the year prior to their request for reopening of their application, with the diagnosis, pathological diagnosis, nature of treatment, and end result.

The next scheduled examination (Part I), written examination and review of case histories, for all candidates will be held in various cities of the United States, Canada, and military centers outside the continental United States, on Friday, Feb. 6, 1953. Application for examination or re-examination, as well as request for resubmission of case reports, must be made to the Secretary prior to Nov. 1, 1952.

Application forms for Appraisal of Incomplete Training, for Certification, and requests for Bulletins should be made to:

ROBERT L. FAULKNER, M.D., SECRETARY
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